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Low Flow / Optimized Flow Oxygen Systems for Passengers

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Technical Report Documentation Page

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12. Abstract The OFOS study evaluated SpO2 values and oxygen flow rates via FAA-approved phase-dilution passenger oxygen masks at simulated cabin altitudes between 12K' and 45K'. Results favor establishment of performance-based, physiological criteria (e.g., range of SpO_2 values) that can be used as a minimum performance standard for the minimum mass flow of supplemental oxygen to a passenger mask for adequate hypoxia protection. OFOS data demonstrate significantly higher stable human blood oxygenation levels are maintained through use of a phase-dilution passenger oxygen mask than is required by 14 CFR 25.1443(c)(2) regulation, and a brief transit as a passenger to 45k' while breathing oxygen from a PAX mask is tolerable (SpO_2 does not fall below 14 CFR 25.1443 (c)(2) regulation guidelines). OFOS data support, 1) 14 CFR 25.1443(c)(2) regulation modification in favor of SpO2 focus, 2)use of less oxygen as a result of SpO2 focused findings, 3) fuel/cost-savings, 4) less CO2 emissions, and 5) evidence that passengers are adequately protected under circumstances of a gradual decompression to 45K' pressure-altitude if exposed for less than 1 minute (validation of FAA Memorandum ANM-03-112-16 (24 MAR 2006)). As a result of this evidence, if more aircraft are type-certified for 45K' flight, then overall safety will improve as a result of decongested NAS national airspace.		
13. Key Word Passenger Oxygen Mask Continuous Flow Pressure Altitude Hypobaric Chamber Tracheal Partial Pressure 8025A Ernsting 25.841 25.1443 TSO C64a Decompression TPP Blood Saturation SpO2 45000 45k hematocrit hemoglobin physiology AS5722 human PAX		14. Distribution Statement Approved for public release Document is available to the public through: National Transportation Library: https://ntl.bts.gov/ntl
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Conflicts of Interest - PAX masks were provided by Safran Aerosystems. However, FAA CAMI utilized this mask system as a surrogate for all phase-dilution oxygen masks and did not endorse any specific masks provided.

Author Contributions
Dr. James E. Campbell: (Conceived design of work, acquired/analyzed/interpreted data, drafted work including substantial intellectual content, approved final version for publication, agreed to be accountable for all aspects assuring accuracy & integrity, has confidence in the integrity of co-author efforts and contributions)
Dr. Susan M. Jay: (Conceived design of work, acquired/analyzed/interpreted data, drafted work including substantial intellectual content, approved final version for publication, agreed to be accountable for all aspects assuring accuracy & integrity, has confidence in the integrity of co-author efforts and contributions))

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List of Abbreviations

Acronym	Abbreviation Explained
AAM	Aerospace Medical Research Division
BMI	Body Mass Index
BPM	Breaths per Minute
BTPS	Body Temperature Pressure Saturated (37°C, ambient pressure, 100% water vapor)
CAMI	Civil Aerospace Medical Institute
cc	Cubic Centimeter
CEVIS	Cycle Ergometer with Vibration Isolation System
CFR	Code of Federal Regulations
CO_2	Carbon Dioxide
DCS	Decompression Sickness (a.k.a. Decompression Illness)
ELOS	Equivalent Level of Safety
EMT	Emergency Medical Technician
FAA	Federal Aviation Administration
ft or ‘	Feet
Hb	Hemoglobin
HCT	Hematocrit
hPa	hectopascal
HR	Heart Rate (beats per minute)
IO	Inside Observer (inside chamber during “flight”)
K’	X1000 feet
L	Liters
LPM	Liters per Minute
m	Meters
min	Minute
mL	Milliliters
mmHg	Millimeters of Mercury

MPS	**Minimum Performance Standards**
N_2	**Diatomic Nitrogen**
NTPD	**Normal Temperature Pressure Dry (20°C, 1 atmosphere pressure, negligible moisture**
O_2	**Diatomic Oxygen**
OFOS	**Optimized Flow Oxygen Systems_Project/Study Title**
PAX	**Passenger Oxygen Mask**
PI	**Principal Investigator**
PO_2	**Partial Pressure of Oxygen**
SAE	**SAE International (formerly the Society of Automotive Engineers)**
SpO_2	**Blood Oxygen Saturation Level (peripheral site: finger)**
TPP	**Tracheal Partial Pressure**
TSO	**Technical Standard Order**
°C	**Temperature in degrees Celsius**
°F	**Temperature in degrees Fahrenheit**

Executive Summary

Primary Scope - The Federal Aviation Administration (FAA) seeks to move away from prescriptive-based standards to more physiologically relevant, performance-based standards such as blood oxygen saturation level (SpO_2) to better assess aircraft passenger safety in addition to providing an easier template for oxygen systems manufacturers in which to abide. Furthermore, the FAA seeks to re-evaluate volume of oxygen flow (LPM) necessary to maintain passengers' blood oxygen saturation levels. Curve "C" as described by the SAE AS8025A document will be generated in support of said re-evaluation.

Secondary Scope - This research investigated passenger oxygen mask (PAX) function and oxygen mask flow rates to maintain adequate SpO_2 levels in human subjects in an altitude chamber up to 45,000 feet (ft) for reasons that 14 CFR Section 25.841 currently limits the cabin pressure-altitude to 40,000 ft yet FAA Memorandum ANM-03-112-16 (24 MAR 2006) currently places that maximal potential decompression event at 45,000 ft. Several airplane manufacturers have been granted exemptions which allow cabin pressure altitudes up to 45,000' following certain failures not shown to be extremely improbable, such as engine rotor failures on aircraft with wing mounted engines. Amendment 25-87 revised the "pressurized cabin" airworthiness standards for subsonic transport airplanes with three new requirements governing cockpit/cabin environment:

- § 25.841 (a)(2)(i) – Cabin pressure-altitude not to exceed 25,000 ft for more than two minutes
- § 25.841 (a)(2)(ii)- Cabin pressure-altitude not to exceed 40,000 ft for any time
- § 25.841 (a)(3) - Fuselage, structure, engine and system failures are to be considered in evaluating the decompression

Potential Beneficial Outcomes – Currently, the minimum performance levels for passenger oxygen systems on transport airplanes resides in 14 CFR 25.1443 which describes the minimum performance levels as a function of tracheal oxygen partial pressure. Since tracheal oxygen partial pressure is not easily measured, it is typically simulated for certification purposes with use of a breathing machine. The Optimized Flow Oxygen Systems (OFOS) study will produce data, analyses, and recommendations that may support future rule-making efforts. Positive findings regarding the primary and/or secondary scope will be used in the certification process for new and existing passenger oxygen systems. This research will add to the collective scientifically founded momentum to justify a rule-making session that favors use of empirical physiological data in lieu of engineering/mechanistic/computer science calculations of oxygen supply adequacy that are currently used and required per FAA doctrine. As a result, current and future oxygen system technologies may experience less restrictive certification regimes. A minimum safe level of human oxygenation based on physiologically relevant, performance-based standards will then be the appropriate focus rather than expected or calculated (i.e., prescriptive) safe levels of oxygen.

Introduction

Title 14 Code of Federal Regulations (14 CFR) Section 25.1443(c)(1) and (2) Minimum Mass Flow of Supplemental Oxygen stipulates that *passenger oxygen equipment* (including masks) must maintain, during inspiration, an average oxygen tracheal partial pressure (TPP) at various cabin pressure-altitudes. Per the regulation, at cabin pressure-altitudes above 10,000 ft up to and including 18,500 ft, a mean oxygen TPP of 100 millimeters of mercury (mmHg) is required when breathing 15 LPM, body temperature 37°C (98.6°F), ambient pressure and gas saturated with water vapor (BTPS), and with a tidal volume of 700 cubic centimeters (cc) with a constant time interval between respirations. A mean oxygen TPP of 100 mmHg is approximately equivalent to breathing air at 10,000 ft. Additionally, according to this regulation, at cabin pressure-altitudes above 18,500 ft up to and including 40,000 ft, a mean oxygen TPP of 83.8 mmHg is required when breathing 30 LPM (BTPS), and with a tidal volume of 1,100 cc with a constant time interval between respirations. Equation 1 (Eq. 1) below provides an altitude (meters; m) to pressure (hectoPascals; hPa) conversion. Conversion into mmHg directly follows in Equation 2 (Eq. 2) to promote familiarity with units in FAA regulations. Calculation of TPP requires equation 3 (Eq. 3) where water vapor pressure is 47 mmHg at body temperature of 37° C and O_2 concentration is 20.95% in air (0.2095 input).

For example, an altitude of 4267.2 meters (14,000 ft) in Eq.1 yields 595.1 hPa which yields 446.36 mmHg via Eq.2, which in turn yields a TPP of 83.7 mmHg oxygen via Eq.3; thus 14,000 ft altitude is equivalent to a TPP of 83.7 mmHg oxygen.

$$barometric\ pressure\ (hPa) = 1013.25 \left(1 - \frac{h\ meters}{44307.694\ meters}\right)^{5.25530} \quad \text{(Equation 1)}$$

$$pressure\ (mmHg) = pressure\ (hPa) * 0.7500616 \quad \text{(Equation 2)}$$

$$TPP\ (mmHg) = barometric\ pressure\ (mmHg) - water\ vapor\ pressure\ (mmHg) * O2\ conc.\ (mmHg) \quad \text{(Equation 3)}$$

As of 2025, 14 CFR § 25.1443 was issued over 60 years ago. Tracheal partial pressure, the main variable in determining adequate oxygen supply for passengers, was established with an estimated continuous oxygen flow rate yet is variably consumed depending on physiological performance needs and body size. Calculations of passenger oxygen needs begin to break down at 41,500 ft as adequate partial pressure of oxygen needed can no longer be established with available ambient air pressure even if 100% oxygen is supplied.

Furthermore, a scientific explanation for selecting 100 mmHg and 83 mmHg oxygen TPP values was not found after an extensive literature search. A 2008 Aviation Safety magazine article (Turner, 2008) reports the account of Dr. Jack Hastings, recipient of the 2016 Louis H. Bauer Founders Award, Fellow and Past President of the Aerospace Medical Association. Dr. Hastings stated that the original requirement “was going to be 10,000 ft” for full-time oxygen use. Flight physicians added that, according to Dr. Hastings, “12,500 ft (without supplemental oxygen) is

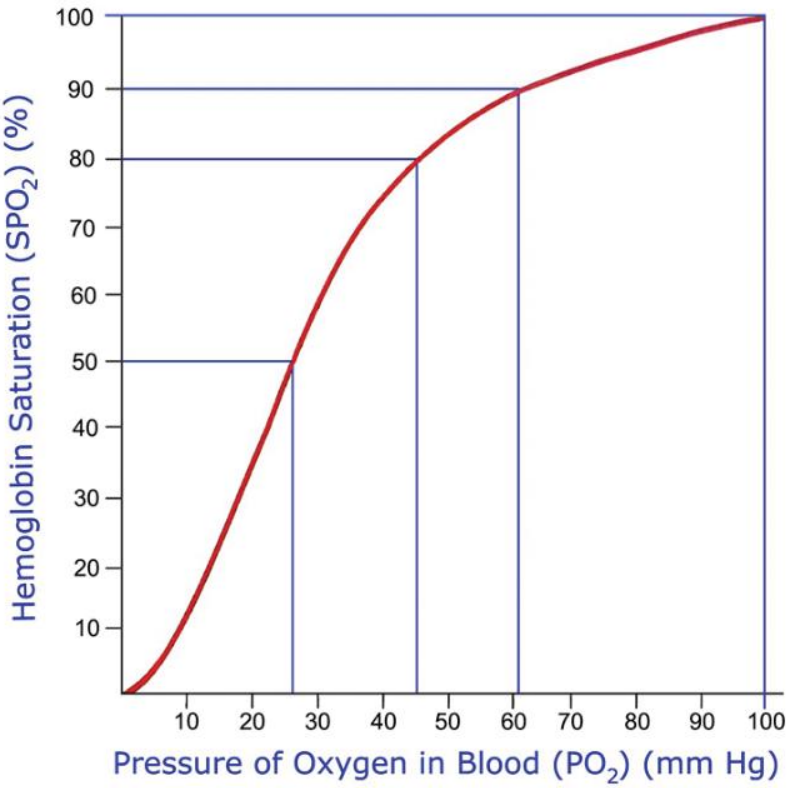
okay for most people." Dr. Hastings also recounted that Dr. John Ernsting, considered the father of modern aviation physiology, "urged that we consider 6000 ft as a minimum" altitude for required oxygen use. Although the Aviation Safety article focused on 14 CFR part 91 general aviation safety, the foundations for 14 CFR part 135 (commuter and on-demand operations) and 14 CFR part 121 (domestic, flag, and supplemental flight operations) are plainly visible in this vignette. Aviation physiology legends worked in tandem with the FAA and industry to generate oxygen rules for safety with the intention and understanding that time at altitude was also a factor and unnecessary restrictions would be costly and inconvenient.

It is apparent that a great deal of subjective input culminated into what is today's definition of "safety" and "hypoxia" in the context of current FAA regulations that pertain to an adequate oxygen supply at altitude. These definitions remain debatable to this day.

Dr. Ernsting stated that "in seated **passengers**, it is acceptable in an emergency to allow the degree of hypoxia induced by breathing air at 15,000ft" equal to an "alveolar PO2 of the order of 45 mmHg."(Ernsting, 1965) On the oxygen-hemoglobin dissociation curve (Figure 1), a PO_2 of 45 mmHg correlates closely with an 80% SpO_2.(Madan, 2017) A combined understanding of the introductory paragraphs therefore culminates in the realization that § 25.1443 veritably requires passengers and cabin attendants to be supplied with oxygen that is equivalent to breathing air at 14,000 ft.

Figure 1

Oxy-Hemoglobin Dissociation Curve.



Passenger (oxygen) masks are currently certified using a breathing machine which simulates TPP with the assumption that the passenger is breathing a homogeneous gas mixture throughout their breathing cycle. Continuous flow phase-dilution masks, the type of mask that is currently incorporated on most commercial airlines oxygen systems and the mask used in this study, capitalize on anatomical features and physiological knowledge of human lung function and dimensions. Oxygen is preserved from waste during human exhalation by being collected into a reservoir bag. This oxygen, when inhaled, is not only doubled in amount delivered as compared to a nasal cannula methodology but remains as 100% oxygen in the early inhalation phase thereby delivering a greater oxygen concentration to the alveolar space. Large dimension passengers, depending upon the size of the passenger's lungs, receive a lower concentration of oxygen to the dead space (bronchioles, bronchi, and upper respiratory structures) that is of significant benefit if the reservoir bag is overbreathed. Greater oxygen delivery to the human anatomical location of oxygen diffusion results in greater oxygen uptake. Actual human condition (blood oxygenation level maintenance) improvements are difficult to accurately capture and describe by current FAA measurement guidelines. Therefore, the FAA desires to move away from the current prescriptive-based measures (i.e., calculated mean TPP values used in combination with a breathing machine) and move towards physiologically relevant, performance-based (e.g., SpO_2 range) for oxygen systems certification that more accurately measure the intended level of hypoxia protection.

Oxygen mask manufacturers/applicants have developed new test methodologies using human subjects and pulse oximetry to determine the minimum oxygen flow to the mask for the user to maintain SpO_2 equivalent to breathing air at the regulatory pressure-altitude. Although manufacturers' proprietary data cannot be reported here, FAA physiologists and engineers have reviewed findings from several commercial entities and agree that appropriate research techniques were employed, and the data generated are likely accurate. Independent testing/ evaluation is needed by the FAA to determine if such data can be used to substantiate a revision to the regulations to define a more performance-based minimum level of hypoxia protection for passengers. Currently, oxygen mask manufacturers/applicants typically meet the minimum performance standards (MPS) qualification and documentation requirements in SAE Aerospace Standard AS8025A (Passenger Oxygen Mask) for airplane passenger oxygen mask certification, stipulated in the FAA's Technical Standard Order (TSO)-C64a (Passenger Oxygen Mask Assembly, Continuous Flow). There are provisions within TSO-C64b (see section (3)(c) Deviations) whereby oxygen mask manufacturers/ applicants may use alternate or equivalent means of compliance to meet the MPS criteria, but if the manufacturers/applicants invoke these provisions they must show that their oxygen equipment maintains an equivalent level of safety (ELOS) to the current, FAA-certified oxygen systems.

This OFOS study seeks to assist the FAA in establishing performance-based physiological criteria (e.g., range of SpO_2 values) that can be used as a minimum performance standard for the minimum mass flow of supplemental oxygen to a passenger mask for hypoxia protection.

To establish physiologically relevant minimum performance values, continuous flow, phased-dilution passenger oxygen masks (i.e., yellow "Dixie Cup") that meet minimum FAA performance requirements defined in § 25.1443 (without the use of ELOS findings) were used with

instrumentation that precisely controlled oxygen delivery to the masks at pressure-altitudes between 12,000 ft and 45,000 ft. Supplemental oxygen flow was provided and adjusted while collecting peripheral SpO_2 values (index finger) to ensure the desired minimum level of hypoxia protection. All test data and technical reports will be publicly accessible via the National Transportation Library's Repository and Open Science Access Portal (ROSA P) website (https://rosap.ntl.bts.gov/)

Study Purpose / Research Objectives

Primary Purpose/Objective A1 - determine SpO_2 values associated with oxygen flow rates for FAA-approved/certified passenger phase-dilution oxygen masks at pressure-altitudes between 12,000 ft up to and including 45,000 ft. These values will be compared against regulation standards.

Secondary Purpose/Objective A2 - Determine the amount of oxygen needed via continuous flow, phase-dilution oxygen systems for participants to maintain his/her own base line SpO_2 value (either 10K' or 14K' according to regulation) at pressure-altitudes between 12,000 ft up to and including 45,000 ft. If the time-limit allows, then the amount of oxygen needed via phase-dilution oxygen systems to participants (mock passengers) at pressure-altitudes between 12,000 ft up to and including 45,000 ft to establish an 80% SpO_2 will be determined. Curve "C", as described in SAE 8025A, will subsequently be generated thereby illustrating "Added Oxygen Flow to Mask LPM NTPD/Cabin Altitude (x1000) ft" relationships to ascertain required minimal performance.

Purpose Summary (Scope of Research) - This "Optimized Flow Passenger Oxygen System" study seeks two primary goals:

> **1)** to assist the FAA in establishing performance-based, physiological criteria (e.g., range of SpO_2 values) that can be used as a minimum performance standard for the minimum mass flow of supplemental oxygen to a passenger mask for hypoxia protection, and
> **2)** determine if a sufficient level of protection could be provided to passenger cabin occupants (i.e., hypoxia protection) using SpO_2 values in lieu of the minimum mass flow rates required per § 25.1443(c)(1) and (2).

This study has a hypothesis-driven SpO_2 -based component as described and various descriptive components that are not hypothesis-driven (minute ventilation, breathing rate, & heart rate) and therefore not statistically evaluated for significant differences.

Materials and Methods

Participants

Potential participants were solicited with focus upon the aviation community. Age groups 18-29 years, 30-39 years, and 40-50 years each contained four acceptable subjects (2 men/2 women) at the conclusion of testing. Healthy women and men between and including the ages of 18 and 50 that possessed a current FAA 3rd class medical certificate or higher (non-expired on the day of experimentation) were recruited for primary reasons of familiarity with aviation and associated phenomena. The OFOS study analyzes data from twelve consented Subjects that experienced the same research protocol. Research subjects were exposed to simulated “flights” in the CAMI research blue hypobaric chamber with one human subject and one Inside Observer occupying the chamber for each flight.

All potential participants were briefed on the procedures, risks and benefits of the study before Informed Consent forms (Appendix B) were signed and official Subject status was granted. A copy of the protocol was provided to each potential participant many days prior to his/her arrival at the research facility. Each potential participant was therefore given ample opportunity to read the protocol and to ask questions prior to signing.

As all Subjects had an FAA class medical as a requirement for participation, no further medical examination was mandated, yet health history questionnaire and pre-flight exam data were collected to assure appropriate preparation was performed, i.e.) unpressurized flight benefits from an appropriate diet, lifestyle and current decongested health status (Appendix A1 and A2). The Principal Investigator interviewed potential participants upon his/her arrival to verify fitness to participate. A participant would be excluded for reasons of inability to clear ears (Valsalva maneuver), respiratory or head/sinus/ear congestion, running a temperature above 99.0 degrees Fahrenheit or any other finding that may jeopardize the research flight or potential participant’s health.

Equipment/Instrumentation

1) Weight Scale (Continental Scale Corp., Health O Meter)
2) Hematology Analyzer: Stat Profile Prime Plus, Nova Biomedical
    a. Hemoglobin and hematocrit testing
3) Blood collection supplies:
    a. Pro-Vent Arterial Blood Sampling Kit with dry lithium heparin, Smiths medical, 4599P-1
    b. Prevent HT Safety Winged Infusion Set (hinged), McKesson, mfr#4666
4) Heart Rate
    a. H10 chest strap, Polar
    b. Vantage V3 wristwatch, Polar, displayed altitude/time/heart rate

c. Signal maximized for electrical conduction with human subject via electrode gel, Spectra360, Natus #016-401800

5) Pulse Oximeters

   a. Nonin Onyx Vantage II Model 9590 – used during medical screening and during chamber flight for Inside Observer to follow Subject's oxygenation level in real time

   b. Nonin Xpod® SpO_2 oximeter 3012LP (external pulse oximeter integrated into Hans Rudolph SmartLab system with PureSAT® signal processing and PureLight® sensor technologies, clinically validated for use with motion and low perfusion) – *used during chamber flight with an adult flex finger sensor (SpO_2 infrared emitter and receiver; Nonin, model 8000J-3 with disposable finger flexwrap, model 8000JFW)*

6) SpO_2, Respirometry and Pressure Sensor Instrumentation

   a. HansRudolph system and associated components

      i. SmartLab Main Sub Assembly

      ii. SmartLab Barometric MOD 15PSIA sensor

      iii. 3830C Pneumotach and 37C warmer

      iv. Natus XactTrace RIP respiratory belt system (abdomen and thorax)

      v. SmartLab SpO_2 sensor system and associated parts

         1. Adult flex finger sensor 3m (SpO_2 infrared emitter and receiver) (Nonin, model 8000J-3 with disposable finger flexwraps)

      vi. SmartLab Spirometry software

7) Respiratory Gas (O2, CO2, N2, Argon) Analyzers (2) (MA Tech Services, Inc.; MATE MGA 1100 with Sample Altitude Manager (SAM) unit) – respiratory gas mass spectrometer

   a. One MATE MGA 1100 unit with sampling line originating inside the altitude chamber to collect ambient chamber air during flight profile

   b. One MATE MGA 1100 unit with sampling line originating inside participant's passenger oxygen mask to collect inhaled and exhaled respiratory gases during flight profile

8) Exercise Bike (Rogue Fitness, (fan) Echo Bike V3.0)

9) Altitude (hypobaric) Chamber (Environmental Techtonics Corporation [ETC])

10) Passenger Oxygen Mask (AVOX SYSTEMS 289-601-066-1 provided by Safran, Aerosystems)

11) Passenger Oxygen Supply System – designed and constructed in-house by Principal Investigator

a. Oxygen tank; Breathing oxygen type 1, Aviators, MIL-PRF-27210G, 99.9% oxygen and 1.3 ppm moisture by analysis (Airgas)

b. Multi-stage pressure regulator for oxygen supply (Harris, 9296ss)

c. Adaptors

d. High-pressure hard nylon tubing (McMaster Carr, 5173K48)

e. Mass flow controller (AliCat Scientific, MC-5SLPM-D) - oxygen delivery control; controls oxygen flow rate from gas cylinder located outside the altitude chamber to the participant's passenger oxygen mask

f. Mass flowmeters (2) (AliCat Scientific, M-5SLPM-D) - oxygen delivery assurance

12) (Fixed Wing) Aviator Helmet (GENTEX, HGU-55/P bungee-visor)

13) Aviator Oxygen Mask (GENTEX; MBU-20/P)

14) Chamber-Mounted, Diluter-Demand Oxygen Stations and CRU-72 Oxygen Regulator with CRU-60 Adapter – connects to MBU-20/P aviator oxygen mask; used by Inside Observer (for duration of chamber flight) and test participants (for ascent from site level to 30K' pressure-altitude)

15) Data Acquisition and Scientific Instrument Hardware (i.e., computers) and Software

a. Dell OptiPlex 7080 small/micro

b. LabVIEW data acquisition software (National Instruments, 2020 version or more recent)

i. Control oxygen supply

ii. Receive, display in real-time and compile all data in 40ms intervals (25Hz)

c. Altitude chamber instrumentation integrated for real-time following (safety and appropriate conduct of experimental processes) and data capture

Passenger Oxygen Mask

An AVOX SYSTEMS 289-601-066-1 (Safran Aerosystems, manufactured April 2024) passenger oxygen mask (PAX) with performance classification code 05152031 – 40 was used in this study. Per AS8025A, the eight-digit performance classification code is assigned to each class of masks and represents the required minimum oxygen flow rates in LPM at normal temperature pressure dry (NTPD) to be delivered to the mask at cabin pressure-altitudes of 15,000 feet (15K'), 25K', 30K', and the maximum approved pressure-altitude. The oxygen flow rates are listed to one decimal point and are derived from performance curves (i.e., "C curves") by testing the mask on a breathing machine.

Example) Performance classification code "AS 8025-08233248-YY-XX" translates to:

0.8 - required minimum oxygen flow, LPM, NTPD, at 15 000 ft

2.3 - required minimum oxygen flow, LPM, NTPD, at 25 000 ft

3.2 - required minimum oxygen flow, LPM, NTPD, at 30 000 ft

4.8 - required minimum oxygen flow, LPM, NTPD, maximum approved pressure-altitude

YY - Maximum approved pressure-altitude in thousands of feet

XX - Additional coding which the mask manufacturer may desire to add

Thus, for the AVOX SYSTEMS 289-601-066-1 PAX used in this study, with performance classification code 05152031 – 40, the minimum oxygen flow rates were:

0.5 - required minimum oxygen flow, LPM, NTPD, at 15 000 ft

1.5 - required minimum oxygen flow, LPM, NTPD, at 25 000 ft

2.0 - required minimum oxygen flow, LPM, NTPD, at 30 000 ft

3.1 - required minimum oxygen flow, LPM, NTPD, at 40,000 ft (maximum approved pressure-altitude of for this mask)

Statistical Product and Service Solutions (SPSS) Statistics software utilized the aforementioned inputs of oxygen flow per pressure-altitude, including a lowest value of 0.0 LPM for 10,000 feet, for non-linear modeling functions TREND and LINT (Transform → Compute Variable) for interpolation/ extrapolation of minimum oxygen flow rates for the additional experimental pressure-altitudes selected in the spirit of AS8025A section 6.1.8 spacing of not more than 7500 ft of separation:

0.25 - minimum oxygen flow, LPM, NTPD, at 12 000 ft

0.83 - minimum oxygen flow, LPM, NTPD, at 18,500 ft

1.17 - minimum oxygen flow, LPM, NTPD, at 20 000 ft

2.55 - minimum oxygen flow, LPM, NTPD, at 35,000 ft

3.24 – minimum oxygen flow, LPM, NTPD at 45,000 ft

The above 9 separate altitude/oxygen flow scenarios comprised that which was delivered to satisfy **Objective 1** of this study.

Objective 2 was investigated through methodical decrements of oxygen flow beginning with the “prescribed” value of Objective 1 and subsequently supplying 75%, 50%, 25% and/or 0% in attempts to generate a curve of SpO_2/scenario data that would capture appropriate oxygen delivery to achieve an 80% SpO_2.

Altitude Hypobaric Chamber Support Personnel

1) Chief Observer (1); FAA AAM-400 member; directed chamber flight from control booth
2) Chamber Operator/Recorder (1); CAMI Airman Education (AAM-400) member; “flew” the chamber as the Chief Engineer from control booth, also recorded flight profile parameters on Flight Run Sheet (e.g., flight altitude, time at altitude, chamber ascent/descent rates)

3) Medical (Med) Deck Supervisor/Principal Investigator (1); CAMI Research Physiologist (AAM-631); responsible for overall conduct of the experimental protocol and chamber flight, test participant and staff safety, and test equipment/instrumentation

4) Inside Observer (IO) (1); required for hypobaric chamber flights, “flew” inside the altitude chamber as a safety monitor for test participants, assisted test participants with experimental tasks

5) Medical Monitor (1); certified and licensed Emergency Medical Technician (EMT) who remained outside the altitude chamber during the entire testing session, ready to provide medical care in the event of an injury or medical emergency

Restroom breaks, part fixing/acquisition, etc. were allowed in minimal and intelligent fashion; not during ops above 30K’. A post-exercise (during 100% oxygen pre-breathe procedure) snack was available (but not promoted since loading the stomach and intestines immediately before ascent was not recommended) and post-flight snack was provided. Water was available and promoted for consumption at any point during experimentation provided that the Investigator considers and establishes that need was greater than risk of mistakes/safety, i.e.) not during 45K’ flight and not during SpO_2 stabilization periods, etc. The Med Deck Sup/Investigator spent a majority of his/her time at the site of experimentation. All personnel were responsible for assisting with setup, testing, and breakdown/cleaning.

Test Procedures

Check-in, Informed Consent, and Initial Screening

Once a potential participant was recruited and scheduled, they received a Pre-flight Subject Exam and Instructions Form (Appendix B) and a copy of the test protocol several days prior to their arrival at CAMI to familiarize themselves with the testing procedures and flight profile. Participants were to refrain from alcohol, exercise, and caffeine for 24 hours prior to testing. If a participant normally ate breakfast, they were encouraged to eat a carbohydrate-rich, but protein and fat-poor breakfast on the morning of testing.

A FAA Third Class (or higher) Medical Certificate was required and witnessed upon arrival by the PI for study participation; thus, no further medical examination was performed. However, on arrival at CAMI the participant submitted the Health History Questionnaire (Appendix A1). The PI interviewed the participant to verify their “testing day” fitness (i.e., medical history, recent blood donation, current medications, vigorous exercise capability, appropriate clothing [exercise clothes/loose fitting attire], no beards/facial hair [to ensure a good oxygen mask fit/seal], etc.). A potential participant was excluded from the study if they could not clear their ears (i.e., Valsalva maneuver), had respiratory or head/sinus/ear congestion, or any other physical finding that could jeopardize the participant’s health during the chamber flight.

Potential participants were briefed by the PI on the OFOS study risks and benefits, that the study was voluntary, rights of the participant including withdrawal without penalty, injury prevention and insurance coverage, confidentiality, cost/compensation, alternative procedures or courses of treatment if necessary, inclusion and exclusion criteria and a full description of

participant involvement. If any questions persisted beyond this briefing, all were answered to the satisfaction of the potential participant immediately and continuously.

If a potential test participant voluntarily signed the Informed Consent designating their willingness to participate, understanding of the OFOS protocol, and they successfully passed the initial screening process, they were formally enrolled in the study (as designated by participant's signature upon the Informed Consent Form: Appendix B). Subject then advanced to the pre-flight physiological screening and completion of Appendix A2 – Pre-flight Subject Exam.

Pre-Flight Physiological Screening

The participant's height and weight were obtained to calculate body mass index (BMI). Less than 25 milliliters (ml) blood sample was collected by arm venipuncture (Pro-Vent Arterial Blood Sampling Kit; Smiths Medical #4599P-1) that was used on occasion in tandem with the Prevent HT Safety Winged Infusion Set [hinged] (McKesson, mfr#4666). Subject's blood was analyzed for Hb and HCT (Nova Biomedical; Stat Profile Prime Plus). If the participant met the pre-flight physiological screening/inclusion criteria (BMI $\leq$ 40, Hb $\geq$ 12.0 g/dL, and HCT $\geq$ 37%), he/she advanced to the altitude chamber for pre-flight test instrumentation, pulmonary function test, and flight equipment fitting.

Pre-flight Test Instrumentation, Pulmonary Function Test, and Flight Equipment Fitting

Upon arrival at the altitude chamber, Subject was instrumented for the collection of heart rate, ventilation/respiration, and SpO_2 data. Subject donned a heart rate monitor chest strap (Polar, H10) that allowed monitoring and data capture throughout the experiment (backup heart rate signal) as well as real-time visual following via LabVIEW for Subject effort guidance to achieve appropriate exertion level (heart rate) during pre-breathe with exercise portion. The donned wristwatch (Polar, Vantage V3) displayed heart rate in beats per minute, pressure-altitude, time and a stopwatch for the Subject's awareness.

Continuous SpO_2 data were collected via pulse oximetry (left index finger) using an adult flex finger sensor (SpO_2 infrared emitter and receiver) (Nonin, model 8000J-3 with disposable finger flexwraps) that was part of the Hans Rudolph SmartLab system. This infrared sensor also delivered the primary heart rate signal data to LabVIEW that acquired data (list sampling rate) for post-experimental analysis. SmartLab + LabVIEW acquired the data (list sampling rate) and allowed post-flight review and analysis after the captured txt files were transformed into Excel spreadsheets.

The participant was fitted with a respiratory belt system (thorax and abdomen elastic straps) (Natus XactTrace RIP) for the collection of respiratory (breaths per minute [BPM] and minute volume (LPM)) data. Anatomical landmarks were used to place these straps for consistency throughout the study (thorax strap covered the xiphoid process; abdominal strap across the navel). Straps were oriented as close to the transverse plane as possible and adjusted for Subject's girth.

The participant was directed for a good mouth seal and a nose clip was placed to perform a pulmonary function test of 7 tidal breaths/1 maximal breath/3 tidal breaths upon the pneumotach (Hans Rudolph, SmartLab to establish conversion factors for the respiratory belt system/expansion straps. The more accurate pneumotach could not be used during testing due to mask wearing constraints which necessitated use of expansion straps for descriptive analysis of respiratory variables. Therefore, post-experiment value corrections were applied according to ratios of pneumotach data to expansion straps data to ascertain BPM and LPM.

On completion of the pulmonary function test, the PI and Altitude Chamber Support Personnel fitted the participant and chamber Inside Observer (IO) with flight equipment – an aviator's helmet (GENTEX, HGU-55) and aviator's breathing mask (GENTEX, MBU-20/P). A good helmet and mask fit, and mask seal were assured via emergency pressure setting on the regulator to assure no leaks or the experiment was cancelled. The mask and helmet were needed by both the participant and IO to ensure adequate 100% oxygen pre-breathe protocol

- IO used the helmet throughout the entire flight profile; CAMI altitude chamber pilot quick don masks (typically used for most CAMI operations) are inadequate for a flight operations above ~ 32,000'; additionally, although they provide 100% oxygen they have insufficient positive pressure for flights above ~ 32,000'; thus an aviator's breathing mask was needed
- The Subject used an aviator's oxygen breathing mask for the experimental flight profile up to 30,000'; kept the mask to ensure no break in 100% oxygen pre-breathe, swapped MBU-20/P mask for PAX mask at 30,000' because at this pressure-altitude a quick mask change could be performed and unlikely that participant would become hypoxic, provided a gastrointestinal pressure check stop, did not compromise denitrogenation pre-breathe Subject status; re-donned helmet and let MBU-20/P dangle off to the side; therefore, if Subject had difficulty with PAX mask above 30K', IO could pull PAX mask down and "sweep" MBU-20/P mask in place to provide 100% oxygen under positive pressure

Participant 10K' and 14K' Baseline SpO2 Values,

Before entry into the chamber, Support Staff thoroughly briefed the participant and IO by restating several of the physiological principles relevant to hypobaric exposure and explaining procedures/communications utilized in chamber flight operations: gas expansion (ears, sinuses, gut), signs/symptoms of hypoxia, oxygen equipment, Valsalva maneuver, forced ear clear, arrest ascent/descent signal "Level-Off", aviator push-to-speak, back up hand-held comm, appropriate breath-hold for mask release and drinking procedure, appropriate avoidance of breath hold during ascent/descent, emergency procedures.

Using testing methods described in AS8025A as a guide, resting baseline SpO_2 values were obtained for each participant at 10K' and 14K' in an altitude chamber while breathing ambient chamber air. The mask minimum oxygen flow rates are used to meet and maintain these 10K' and 14K' baseline SpO_2 values at various test pressure-altitudes. By using this methodology, the prescriptive-based minimum required TTP values in § 25.1443(c)(1) and (2) may be translated into physiological, performance-based criteria.

Once briefed, the Subject and IO entered the chamber and were seated comfortably at their respective stations. A pulse oximeter (Nonin Onyx Vantage II Model 9590) was affixed to Subject's right index finger by its alligator clip design. Chamber door closed and sealed, comms check, once both the participant and IO affirmed they were ready for ascent, the "baseline values" flight commenced.

Subject breathed ambient chamber air during entire "baseline values" flight; IO donned aviator oxygen mask and breathed 100% oxygen any time chamber pressure-altitude was at and above 10K'

The chamber was ascended at 5,000 ft/min and leveled off at 10K' until the Subject's SpO_2 values stabilized, generally between 5 and 10 minutes. ***Stable SpO_2 values*** were the Subject's "10K' baseline SpO_2" that correspond to a mean TPP of 100 mmHg. Mask minimum oxygen flow rates as stamped on PAX masks are purported to meet and maintain this 10K' SpO_2 baseline at the 12K', 15K', and 18.5K' experimental test pressure-altitudes for which this line of OFOS research intends to investigate.

The chamber was then ascended at a maximum of 5,000 ft/min and leveled off at 14K' until the Subject's SpO_2 values stabilized, generally between 5 and 10 minutes. ***Stable SpO_2 values*** were the participant's "14K' baseline SpO_2" and corresponds to a mean TPP of 83.8 mmHg. Mask minimum oxygen flow rates as stamped on PAX masks are purported to meet and maintain this 14K' SpO_2 baseline at the 18.5K', 20K', 25K', 30K', 35K', 40K', and 45K' experimental test pressure-altitudes for which this line of OFOS research intends to investigate.

Subject's *stable SpO_2 values* - Methodology employed by the Principal Investigator

LabVIEW data acquisition software was programmed to capture 1-minute, 3-minute and 5-minute rolling SpO_2 averages. The PI monitored the participant's SpO_2 values in real time to determine when stability occurred. A stable SpO_2 value was defined as:

- > 97% for 1 minute after rising from a lower SpO_2 value, or
- < 97% for 3 minutes with the caveat that a participant's loss of rhythmic breathing caused anomalous readings.

Yawns, talking, movement (as minimal as a head turn), sighs, and dozing off/sleeping all presented potential perturbations to a stable SpO_2. Therefore, the PI briefed each participant on these interfering factors and requested them to perform comfort adjustments/movement/ talk only during transitions between testing pressure-altitudes, and to focus upon rhythmic breathing similar to tidal volumes during SpO_2 stabilization data collection periods.

Chamber Flight Ear Pressure Check – Occurred Simultaneously with 10K' and 14K' flight

IOs prepared for chamber flight: secured doors, pre-flight tests. Subject and IOs "flew" to 10K' and subsequently to 14K' to establish a stable SpO_2 base line as described above. Following SpO_2 data collection, hypobaric chamber was descended with focus upon Subject's ability to clear his/her ears. Upon reaching ground level, chamber door was opened, pilot masks were

donned, and 100% oxygen breathing began. Time was marked to indicate the start of pre-breathe protocol to assure appropriate total duration (2.5 hours).

In Chamber Pre-Breathe Protocol (continued at ground level)

PI estimated that experimental flight profile would take approximately 3 hours to complete, with a maximum pressure-altitude of 45K', and total time of 2 hours 20 minutes above 18K – all factors that contribute to the risk of altitude decompression sickness (DCS).

Using literature review sources, in consultation with high-altitude physiology/altitude DCS subject matter experts, NASA resources, and the US Air Force Altitude Decompression Sickness Risk Assessment Computer (ADRAC) model, the PI calculated several DCS mitigation options. Ultimately a slightly modified version of NASA's Cycle Ergometer with Vibration Isolation System (CEVIS) Pre-Breathe Reduction Program (PRP) Phase II protocol was selected as optimal for maximal reduction in DCS risk in a short amount of time. Appendix A5 contains a more detailed description of the CEVIS protocol and why it was selected. Appendices A3 & A4 present DCS risk minimization and DCS signs/symptoms, respectively.

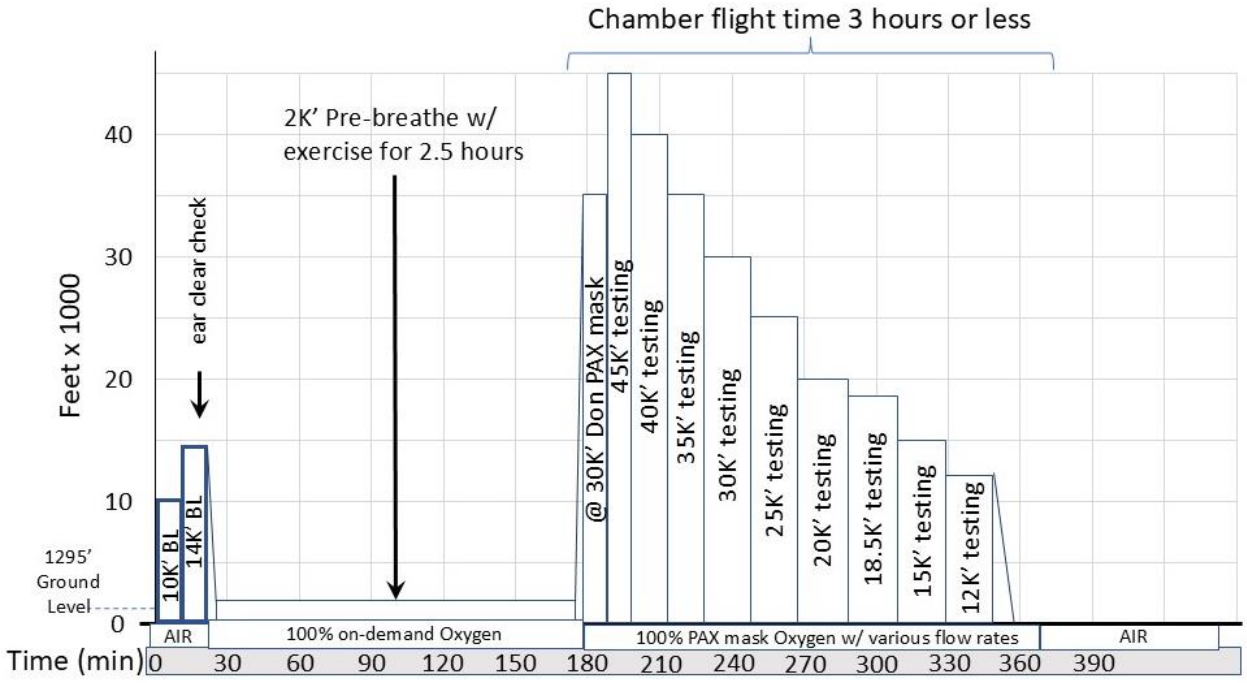
Thus, to minimize the risk of DCS, the participant and IO both completed a 2.5-hour 100% oxygen from pressure-supply masks + exercise protocol consisting of:

- Cycling on an exercise bike (Rogue Fitness; *(fan) Echo Bike V3.0)* at approximately 166 Watts level effort for 10 minutes at (or above) 75% HR_{max} with reaching 85% HR_{max} at least once during the 10-minute exercise bout.
- Seated rest recovery for approximately 35 minutes
- At the 55-minute mark, four rounds of light exercise consisting of gentle stretching of all the major muscle groups (demonstrated and led by PI), plus five minutes of light/easy cycling on the exercise bike
- Seated rest for the remainder of the 150 minute pre-breathe/exercise protocol (approximately 55 more minutes)

Experimental Chamber Flight Profile and Data Collection

Once the 2.5-hour mark for the 100% oxygen pre-breathe + exercise protocol was reached, the chamber was readied for the experimental flight profile (Figure 2). The PI instructed the participant and IO to expend very little physical activity during the flight (exertion at pressure-altitudes over 20k' increases the risk of DCS), thus both the participant and IO remained seated throughout the flight and the IO stood only when necessary. The chamber door was closed and sealed. The Chief Observer performed an "All Crew" communications check and re-briefed the participant and IO on the flight profile and hand signals/"Level-Off" sign, reiterating that they could request a "level-off" at any time for any reason (e.g., discomfort, pain). Once both the participant and IO affirmed they were ready for ascent, the experimental flight commenced.

Figure 2
Altitude Chamber Flight Profile. The independent variables for this protocol are the 9 combinations of pressure-altitude and oxygen flow supplied.



All participants performed the same altitude chamber flight profile in the same sequence, although total time at various pressure-altitudes varied depending on participant's performance (i.e., SpO_2 values). A "total time" limit (as approved by CAMI Institutional Review Board [IRB]) was imposed for each testing pressure-altitude to limit (unpressurized) exposure to high altitude (i.e., minimize risk of DCS, gas expansion, etc.), yet enough time was provided to collect meaningful data (e.g., stabilized SpO_2 values, breathing rates, oxygen flow rates, etc.). The participant's SpO_2 values were monitored and recorded continuously throughout the flight. At every testing pressure-altitude except for 45K', once a stable SpO_2 value was reached for the last testing scenario planned, the PI signaled to the Chief Operator/Recorder and Chief Observer to descend the chamber to the next testing flight altitude.

Experimental chamber flight profile is provided in the detailed outline below. "Data collection" in each bullet point below refers to primary and secondary objectives. Briefly, at each pressure-altitude of 40k' and below, an oxygen flow was initially delivered as "prescribed" by regulations/standards and as stamped on the oxygen mask (Objective 1) and a stable SpO_2 was determined. Subsequently, at each pressure-altitude of 35K' and below, oxygen flow is delivered as "prescribed" AND then decreased by design delivers 75%, 50%, 25% and/or 0% of "prescribed" delivery to again determine SpO2 per experimental scenario. This data was expected to allow generation of a non-linear association of SpO2 vs. altitude/oxygen flow scenario to subsequently define the oxygen flow per pressure-altitude that will result in 80% SpO_2 (Objective 2).

- Ascend chamber from ground level to 30K’ at 5,000 ft/min; level-off at 30K’
    - Exchange participant’s aviator’s oxygen mask with passenger oxygen mask. Passenger mask prepared for use with 100% oxygen flowing at 3.1 LPM (highest flow rate for highest certified mask pressure-altitude) just prior to donning
    - IO assisted participant with mask exchange, ensured good passenger mask face seal, and participant comfort
    - Participant and IO both affirmed readiness to ascend to 45K’
- Ascend chamber from 30K’ to 45K’ at 6,500 ft/min; level-off at 45K'
    - Dwell for approximately 17 seconds, then initiate immediate descent to 40K’ at 10,000 ft/min
    - Descent was timed and automatic
- Level-off at 40K’; data collection, dwell time not to exceed 15 minutes
    - Descend chamber to 35K’ at 5,000 ft/min
- Level-off at 35K’; data collection, dwell time not to exceed 15 minutes
    - Descend chamber to 30K’ at 5,000 ft/min
- Level-off at 30K’; data collection, dwell time not to exceed 20 minutes
    - Descend chamber to 25K’ at 5,000 ft/min
- Level-off at 25K’; data collection, dwell time not to exceed 20 minutes
    - Descend chamber to 20K’ at 5,000 ft/min
- Level-off at 20K’; data collection, dwell time not to exceed 20 minutes
    - Descend chamber to 18.5K’ at 5,000 ft/min
- Level-off at 18.5K’; data collection, dwell time not to exceed 20 minutes
    - Descend chamber to 15K’ at 5,000 ft/min
- Level-off at 15K’; data collection, dwell time not to exceed 20 minutes
    - Descend chamber to 12K’ at 3,000 ft/min
- Level-off at 12K’; data collection, dwell time not to exceed 20 minutes
    - Descend chamber to ground level at 3,000 ft/min
    - IO was allowed to remove aviator’s mask/helmet at 10k’, Subject continued to breathe into PAX mask for entirety of descent

*Note - Time at 45K’ ft was limited to participant SpO_2 performance, risk tolerance for unconsciousness, and logistical challenges such as computer program flight profile progression limitations. In a study by Barron et. al. (1963), ONE 36year-old participant, wearing a Firewel passenger oxygen mask, ascended in an altitude chamber to 44,295 ft in 38 seconds. He lasted

42 seconds at this peak pressure-altitude before the chamber was recompressed due to his SpO_2 (earlobe) reaching a lowest value of 60%. He experienced light-headedness at altitude with no other discomfort. Therefore, a simulated gradual/insidious aircraft decompression was simulated in this OFOS project to ascend cabin pressure at 6,500 ft/minute on unpressurized passenger mask provided oxygen at 3.24LPM to a peak pressure-altitude of approximately 44,750'. Subject dwelled for minimal time (10-20 seconds) for which the chamber operators could maximize safety in preparation and execution of descent to 40,000 ft pressure-altitude for continuation of research.

Post-Flight One Hour "Clean Time", Participant Debrief, and Check-Out

- As part of the DCS mitigation protocol, participant remained on passenger mask supplying 100% oxygen for 5 minutes after return to ground level
- For the first 30 minutes at 10-minute intervals, Subjects were monitored by IOs and/or PI for signs/symptoms of DCS (Appendix A6). Subjects were requested to remain constantly aware of any pain, niggles, anomalies to inform IO/PI/medical monitor of any abnormal personal assessments.
- 60 minutes after return to ground level, Subject released from CAMI with instructions:
    - Refrain from strenuous activity for 12 hours
    - Avoid alcohol consumption for 12 hours
    - Valsalva frequently throughout the night (clear ears and flex torso as if defecating) – Draegar ear was not expected but be aware of inner ear pressure and equilibrate often
    - Be aware of potential signs/symptoms as listed in Appendix A4, review with IOs/PI last thing before departure
        - Report to your employer any signs/symptoms and/or call 911 for medical attention. It was advised that Baptist Integris was informed/utilized for close hyperbaric support and expert medical opinion.
- A post-flight clean hour was required for the participant and IO as part of DCS mitigation protocol, medical monitor was onsite and a majority cases of altitude DCS occur within one hour of returning to ground level

Independent and Dependent Variables

Independent Variable: - nine experimental/test chamber pressure-altitudes with the corresponding oxygen flow rate as specified for that pressure-altitude per the mask performance classification code.

Dependent Variables – Part 1:

1) SpO_2 pulse oximeter readings using FAA-prescribed oxygen flow rates [hypothesis driven research]
2) Respiratory Rate (BPM) and Minute Ventilation (LPM) [descriptive analysis]
3) Heart Rate [descriptive analysis]

Dependent Variable – Part 2:

1) Oxygen flow delivery (LPM) was adjusted to estimate oxygen flow demands via phase dilution passenger masks to maintain SpO_2 base line values (either 10K' or 14K'). Preliminary test plan execution prior to human subject research revealed the near impossibility of tuning oxygen delivery for desired SpO_2. Therefore, oxygen flows were decreased equally per ratio at each pressure-altitude for 75%, 50%, and 25% of initial value, i.e.) 2.0LPM, 1.5LPM, 1.0LPM and 0.5 LPM @ 30,000 ft.

Primary Test Parameters:

1) Blood Measures
    a. Hemoglobin
    b. Hematocrit
2) Blood Oxygen Saturation (SpO_2). Blood oxygen saturation level data were collected via pulse oximetry (e.g., finger oximeter) SpO_2 values are the primary experimental dependent variable of interest.
3) Oxygen gas flow rate (O_2).
4) Pulmonary function data – respiration rate, minute volume
5) Heart Rate

Analysis

Statistical Analysis (SpO_2 Data):

Statistical power determined *a priori* for a one-way repeated measures ANOVA (within subjects) using G*power software that **twelve** research participants were necessary for this study to ascertain effects of prescribed oxygen flow delivery per pressure-altitude upon human blood oxygenation levels as determined by near infrared spectroscopy technology utilized on the human finger (SpO_2). Specifically, this report required n=12 and recruited fourteen (14) individual participants of which 2 participants attended twice due to experimental difficulties/aborts, thereby demanding sixteen (16) total active chamber-flight days of study to collect twelve (12) successful and complete data experiments. According to the following G-power inputs, fifty-four *total test participants* are required to afford a *95% power* with a large effect size (calculated as 0.765 using previously generated data from AVOX), an alpha err probability of 0.05 ($p \leq 0.05$), nine groups (levels of the independent variable, i.e., nine experimental/test chamber pressure-altitudes), a 0.50 correlation factor, and non-sphericity correction of 1.0. As the fifty-four participants are represented over the spread of nine groups, the actual number of participants that are necessary per software calculations is six (54/9). Industry data used for this effect size calculation may be inaccurate and therefore twice the number of human subjects that were calculated in the power analysis will be utilized (six x 2 = ***twelve***) to counteract lack of confidence. Furthermore, this study headed guidance of SAE AS8025A that states "validity of performance tests of this nature shall be demonstrated using at least 11 different human subjects.

Experimentation concluded upon reaching twelve successful experiments (n=12) and the data of these twelve Subjects was used for an appropriately powered analysis using IBM SPSS Statistics software, v.28.0.1.0 (142). Repeated measures – general linear model (RM-GLM) regression with appropriate corrections for main effects was performed and subsequent multiple comparisons were warranted. Measurements were compared using distinct experimental

scenarios 1-9 data against the 10K' or 14K' base line to minimize multiple comparisons to only those necessary to test the hypothesis.

To reiterate, the null hypothesis will be rejected if $p \leq \alpha$ (shown as 0.05 above). Tests will be two-sided. Gender and Age will be tested for between-subject effects.

Hypothesis (H1) – Human blood oxygenation saturation values (SpO_2) that result from the prescribed oxygen flow rates as stamped on aviation passenger masks significantly differ from SpO_2 values that result from requirements within 14 CFR part 25.1443(c).

Descriptive Analysis

1) SpO_2 data were also analyzed descriptively
    a. Curve "C" illustrations were generated according to SAE 8025A document showing the minimal required oxygen delivery per pressure-altitude.
    b. SpO_2 data were utilized to assess risk involved in a simulated emergency decompression that abides by FAA guidance.
2) Hemoglobin and hematocrit – descriptive statistics only (i.e., means, standard error with no statistical comparisons
3) Breathing data (i.e., respiration rate and minute volume) -- descriptive statistics only (i.e., means, standard error with no statistical comparisons).
4) Heart rate data (i.e., beats per minute) -- descriptive statistics only (i.e., means, standard error with no statistical comparisons).

All Data Analysis

Breathing data and heart rate data used for analyses were of the same timeframe of SpO_2 stabilization, i.e.) the last minute of an altitude/oxygen flow scenario. Additional descriptions may be found in Appendix A7 for SpO_2, breathing, and heart rate data analysis.

Results

Participant Demographic, Anthropometric and Clinical Variables Descriptive Data

Fourteen participants were recruited for this study, twelve of whom successfully completed the experimental flight profile. There were 16 altitude chamber flights (i.e., testing session) with four flight aborts – two due to ear blocks (these participants were unable to be rescheduled and did not return), one due to intestinal gas expansion pain on ascent, and one due to an inability to get a good face/mask seal with the aviator's oxygen breathing mask. These last two participants were rescheduled (and additional flight equipment attained) and successfully completed the experimental flight profile. Thus, a total of twelve participants completed the study and their data analyzed -- six males and six females, two each in the following age categories: 18-29 years, 30-39 years, and 40-50 years.

All participants were active pilots who possessed a current, valid (i.e., non-expired) FAA Third Class (or higher) Medical Certificate and a FAA Pilot License and met study inclusion criteria: Body Mass Index (BMI) $\leq$ 40, hemoglobin (Hb) $\geq$ 12.0 g/dL, and hematocrit (HCT) $\geq$ 37%. Table 1 lists participant individual and group average demographic, anthropometric, and clinical variable data. The participants were a representative sample of the U.S. flying public, although the average participant BMI of 27.6, was less than the American public average BMI of 30 (National Health and Nutrition Examination Survey NHANES; 2016 and CDC findings 2021-23).

Table 1

Human Subjects' Demographic, Anthropometric and Clinical Variables Data

sex	m	m	m	f	m	m	f	f	f	f	m	f	avg	sem
age (yrs)	45	27	41	22	36	24	24	46	32	35	32	45	34.1	2.5
height (in)	69	72	73	62	73	74	64	65	63	64	73	66	68.2	1.3
weight (lbs)	179	199	244	111	240	294	118	154	137	172	203	181	186.0	15.7
BMI	26	27	32	20	32	38	20	26	24	30	27	29	27.58	1.43
Hct (%)	48	53	50	44	44	48	46	44	42	43	46	41	45.8	1.0
Hgb (g/dL)	16	19	17	15	16	16	16	15	15	15	16	14	15.8	0.4
rest HR (bpm)	60	70	65	63	75	73	71	57	68	74	45	59	65.0	2.5

Blood Oxygen Saturation Data (SpO2) By Specific Altitude and Oxygen Flow Rate Exposure

Table 2 presents participant individual and group average SpO2 (%) values by flight altitude (ft) and mask oxygen flow rate (LPM), as well as the results of the 1-way repeated measures (RM) ANOVA (General Linear Model [GLM]). Blood oxygen saturation data for each participant are displayed in the order of the experimental flight profile: 10K' and 14K' baseline SpO2, 45K' with maximum oxygen flow rate (i.e., simulated gradual decompression), and the stair-step descent to ground level through the performance classification codes altitudes (40K', 30K', 25K', 15K') with oxygen flow rates as prescribed on the passenger oxygen mask, and the additional

experimental flight altitudes (35K', 20K', 18.5K', 12K') with calculated oxygen flow rates. Group average SpO2 values for each flight altitude and oxygen flow rate are listed in the last column.

Table 2

Participant Individual and Group Average Blood Oxygen Saturation Levels by Altitude and Oxygen Flow Rate

alt	O2 LPM	Subj 1	Subj 2	Subj 3	Subj 4	Subj 5	Subj 6	Subj 7	Subj 8	Subj 9	Subj10	Subj11	Subj12	avg	
10k' BL	0	91	92	87	89	91	90	91	92	93	87	90	90	90.25	
14k' BL	0	81	81	80	85	85	83	82	82	72	76	82	80	80.75	
45k'	3.24	79	76	79	84	83	80	81	84	80	84	84	85	81.58	#
40k'	3.10	96	91	91	98	92	91	95	98	95	97	95	93	94.33	*#
35k'	2.55	99	96	95	100	95	96	98	100	99	98	98	96	97.50	*#
30k'	2.00	99	97	97	99	98	97	99	100	100	99	99	97	98.42	*#
25k'	1.50	99	98	96	98	98	97	99	100	99	99	99	98	98.33	*#
20k'	1.17	99	99	94	98	98	94	99	100	99	99	98	98	97.92	*#
18.5k'	0.83	98	99	95	98	96	93	98	100	99	99	98	96	97.42	*#
15k'	0.50	96	98	94	95	94	92	98	98	98	98	95	94	95.83	*#
12k'	0.25	93	88	95	92	92	91	95	94	97	94	93	92	93.00	*

Note. Statistical results of the one-way RM-GLM ANOVA.

* Significant for altitude and oxygen flow rate combination versus § 25.1443(c)(2) regulation requirement of 14K' equivalent SpO2 baseline ($p < 0.05$)

Significant for altitude and oxygen flow rate combination versus § 25.1443(c)(1) regulation requirement of 10K' equivalent SpO2 baseline ($p < 0.05$)

SpO_2 Statistical Analysis – Altitude/Oxygen Supply Versus 14K' Equivalent SpO_2 Base Line

The 14K' equivalent SpO2 baseline represents the lowest permissible limit (i.e. equivalent to 83.8 mmHg TPP) for adequate passenger oxygenation at cabin pressure altitudes above 18,500 feet up to and including 40,000 feet as prescribed per 14 CFR 25.1443(c)(2).

A one-way repeated measures general linear model ANOVA (RM-GLM; 10 levels, 9 comparisons, simple contrast) (SPSS; software version v.28.0.1.0 (142)) was performed with all dependent variable altitude/oxygen flow rate combination SpO_2 values against this 14K baseline. Altitude/oxygen flow rate inputs were the within-subjects factor; sex and age were the between-subjects factors. Altitude/oxygen flow combinations (labeled ALTITUDE in SPSS analyses) were treated as a single effect as determined a priori. Mauchly's Test of Sphericity ($W = 0.000$) indicated violation of sphericity assumption. This was expected for unequal variances of differences when comparing a baseline SpO2 value to each unique altitude/oxygen flow rate combination. The Greenhouse-Geisser correction showed significance for main effect ($F(2.71, X) = 190.329$, $p < 0.001$). Partial eta squared was 0.969, indicating a large effect size.

Therefore, multiple comparison analyses were performed to determine significant differences for the ALTITUDE main effect using Bonferroni correction. All comparisons were significant ($p <$

$0.00\bar{5}$)(i.e., participant's SpO_2 values were significantly greater than their 14K' equivalent SpO2 baseline) except for the 14K' SpO2 baseline verses 45K' altitude/3.24 LPM oxygen flow rate combination ($p = 0.118$). Furthermore, partial eta squared values of multiple comparisons had significance values ranging between 0.970 and 0.993, providing additional support for an exceptionally large effect size.

These results indicate that, **with the exception at 45K'**, the oxygen flow rates stamped on the passenger oxygen mask provided significantly greater blood oxygenation than the participant's 14K' equivalent SpO2 baseline value (80.75% SpO_2) for all test/flight altitudes. The 45K' blood oxygenation value (81.58% SpO2) was neither significantly greater nor lesser than the 14K' base line SpO2.

SpO_2 Statistical Analysis – Altitude/Oxygen Supply Versus 10,000' Equivalent SpO_2 Base Line

A one-way repeated measures general linear model ANOVA (RM-GLM) was repeated in similar fashion to above against the 10K' base line. The 10K' equivalent SpO2 baseline represents the lowest permissible limit (i.e. equivalent to 100 mmHg TPP) for adequate passenger oxygenation at cabin pressure altitudes above 10,000 feet up to and including 18,500 feet as prescribed per 14 CFR 25.1443(c)(1). Mauchly's test of Sphericity indicated violation of the sphericity assumption (W=0.000). Greenhouse-Geisser main effects of ALTITUDE/OXYGEN FLOW rejected the null hypothesis ($F(2.87, X) = 117.432$, $p < 0.001$) with a partial eta squared of 0.951.

Therefore, altitude/oxygen flow multiple comparisons with Bonferroni corrections subsequently followed for which all were found to be significantly different with the lone exception of the 12K' 0.25 oxygen flowed scenario. 10,000' BL vs. 12k' 0.25LPM oxygen ($p=0.009$) was not less than the Bonferroni corrected (0.05/9) $p \leq 0.00\bar{5}$ and therefore showed no significant difference (SpO_2 not determined to be significantly different than 10k' base line SpO_2 value).

Keep in mind that, in the range above 10K' pressure-altitude but below 18.5K' pressure-altitude, the PAX mask must only provide oxygen equivalent to that which was delivered at 10K' (90.25% SpO_2 in this study). The 12K' prescribed (OFOS calculated 0.25 LPM; 93.00% SpO_2) oxygen flow delivery is not significantly greater or lesser per statistical analysis. Table 3 below shows that 12K' with 0.13LPM oxygen delivery (half of prescribed) resulted in an average 91.2% SpO_2 which presented a similar situation; adequate but not significantly greater blood oxygenation level as compared to the 10K' base line SpO_2 level.

Additionally, to elaborate on the 45K' short excursion significant difference revealed with statistical analysis, a significantly **lower** SpO_2 occurred as a result of that exposure (81.58%) than the 10K' SpO_2 base line (90.25%). This result abided perfectly with regulations because, as mentioned in the above section, this blood oxygenation level met the 14K' SpO2 base line.

SpO_2 Descriptive Analysis and Curve "C" Calculation

Because preliminary/pilot testing showed how difficult it was to "tune" an individual's SpO_2 to a given percentage, the goal of the secondary purpose/objective A2 was to incrementally decrease the flow rate as a fixed percentage (e.g., 75%, 50%, 25%) of the maximum flow rate

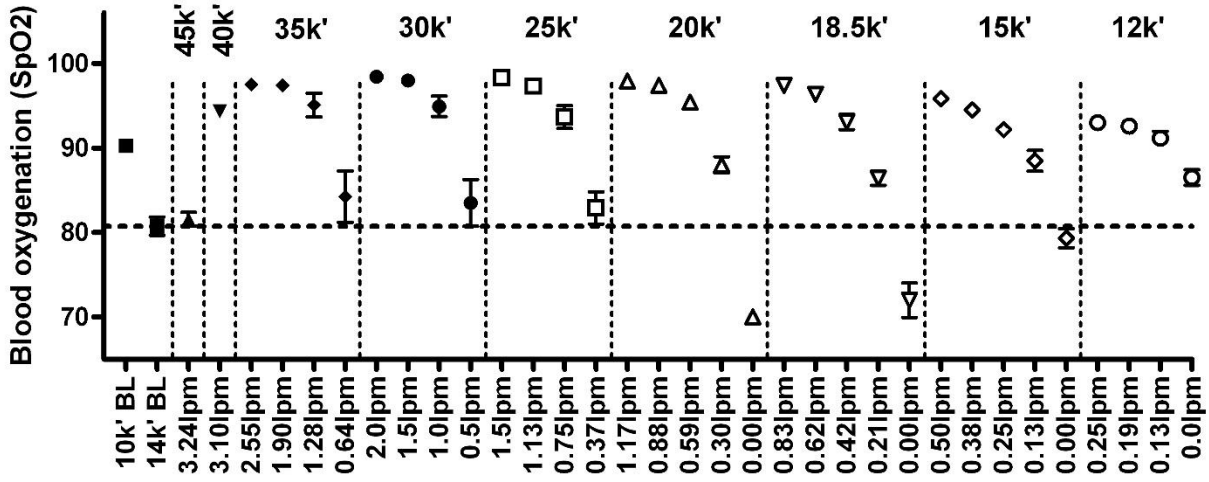
as stamped on the mask at a given altitude and determine what minimum % of flow rate was needed to maintain a participant's SpO_2 value at the group 10K' and 14K' SpO_2 baseline values (90.25% and 80.75% respectively). Of course, group base line values could not have been known and were not known a priori and therefore 25% of prescribed flow was estimated to deliver blood oxygenation values below 80% SpO_2 to then allow for such interpolation of data post-experimentation.

All SpO_2 data of decreasing oxygen supply separated into respective pressure-altitudes are reported (Table3). SPSS analysis of these data provided non-linear curve fitting. Curve "C" generation was accomplished following oxygen flow values correlation with OFOS SpO_2 base line values of 90.25% (Table 4) and 80.75% (Table 5) as found experimentally for 10,000-foot and 14,000-foot equivalence, respectively. Strikingly, oxygen flowed at one-quarter of prescribed values (required/stamped on the PAX mask) continued to provide adequate oxygen to maintain a high enough average human subjects SpO_2 as required by regulation at several altitudes. However, one must note the much higher standard error of the mean associated with this low-volume supply of oxygen where some Subjects maintained near maximal SpO_2 while others were no longer in a "useful" state (Subj 6 @ 35,000' and 0.64LPM oxygen; eyes began to roll up, presyncope state, IO voiced concern for visible sign with 65% SpO2 in this Subject). Additional investigation may reveal that people with larger tidal volumes (large humans with large operating lung volumes at rest) need greater amounts of oxygen in the resting state and are at greater risk of inadequate oxygenation at low oxygen supply volumes. Subject 6 anthropometric, breathing, and heart rate data support this assessment.

Table 3 (with accompanying graph)

Participant Individual and Group Average Blood Oxygen Saturation (SpO_2) Values by Altitude and Decreasing Oxygen Flow Rate

alt	O2 LPM	Subj 1	Subj 2	Subj 3	Subj 4	Subj 5	Subj 6	Subj 7	Subj 8	Subj 9	Subj10	Subj11	Subj12	avg	sem
10k' BL	0.00	91	92	87	89	91	90	91	92	93	87	90	90	90.3	0.5
14k' BL	0.00	81	81	80	85	85	83	82	82	72	76	82	80	80.8	1.1
35k'	2.55	99	96	95	100	95	96	98	100	99	98	98	96	97.5	0.5
	1.90	99	95	97	100	93	96	98	100	99	98	98	96	97.4	0.6
	1.28	98	85	92	99	88	91	98	99	99	98	98	96	95.1	1.4
	0.64	88	72	79	88	82	**65**	97	98	98	88	78	78	84.3	3.0
30k'	2.00	99	97	97	99	98	97	99	100	100	99	99	97	98.4	0.3
	1.50	99	95	97	99	98	95	99	100	99	99	99	97	98.0	0.5
	1.00	97	90	91	91	92	88	99	100	99	98	98	96	94.9	1.2
	0.50	81	71	80	73	77	75	98	92	99	92	81	83	83.5	2.8
25k'	1.50	99	98	96	98	98	97	99	100	99	99	99	98	98.3	0.3
	1.13	99	97	94	96	97	93	98	100	99	99	99	97	97.3	0.6
	0.75	94	85	90	93	94	86	97	100	99	97	95	94	93.7	1.4
	0.37	81	71	82	80	77	76	89	91	94	86	84	84	82.9	1.9
20k'	1.17	99	99	94	98	98	94	99	100	99	99	98	98	97.9	0.6
	0.88	99	98	94	98	96	94	98	100	99	99	98	96	97.4	0.6
	0.59	97	97	93	93	92	91	97	99	99	97	96	94	95.4	0.8
	0.30	86	88	88	85	84	84	91	93	94	89	88	86	88.0	1.0
	0.00												70	70.0	n/a
18.5k'	0.83	98	99	95	98	96	93	98	100	99	99	98	96	97.4	0.6
	0.62	95	97	95	98	95	90	97	99	99	98	98	95	96.3	0.7
	0.42	90	95	92	90	90	89	95	98	98	95	93	92	93.1	0.9
	0.21	83	85	89	85	82	85	88	91	91	87	85	86	86.4	0.8
	0.00							78	76	**64**	**69**	73	72	72.0	2.0
15k'	0.50	96	98	94	95	94	92	98	98	98	98	95	94	95.8	0.6
	0.38	92	96	94	95	92	91	97	99	98	96	91	93	94.5	0.8
	0.25	88	93	94	90	89	91	93	97	96	93	92	90	92.2	0.8
	0.13	83	87	93	85	84	90	98	91	91	87	87	86	88.5	1.2
	0.00							83	80	75	79	81	78	79.3	1.1
12k'	0.25	93	88	95	92	92	91	95	94	97	94	93	92	93.0	0.7
	0.19	91	90	96	90	89	92	94	96	96	93	93	91	92.6	0.7
	0.13	89	88	95	88	89	91	93	96	94	91	91	89	91.2	0.8
	0.00	86	88	95	85	84	87	89	86	83	85	86	84	86.5	0.9



Note (Table 3). Participant individual and group average SpO2 data are presented within an altitude level by decreasing oxygen flow rate from maximum flow rate at that altitude, 75% of maximum flow rate, 50% of maximum flow rate, and 25% of maximum flow rate. Low SpO2 values (< 70%) are emphasized with dark gray background and bold print. Horizontal dashed line indicates 14K' SpO2 equivalent. Vertical dashed lines separate experimental altitudes as specified at top of graph. Table 3 data are presented in the accompanying graph as group SpO2 (mean + standard error of the mean [SEM]) by altitude (K') and oxygen flow rate (LPM).

To reiterate a page 15 note - time at 45K' ft was limited to participant SpO_2 performance, risk tolerance for unconsciousness, and logistical challenges such as computer program flight profile progression limitations. At the 45,000-foot cabin pressure-altitude, it is widely reported in the literature and accepted as fact that no oxygen flow provision possibility will maintain SpO_2 above the experimentally established 80.75% 14,000 base line equivalence unless delivered with positive pressure. Rather extreme time-limitation is supported by OFOS data as described in the following section and supported by lack of significant difference found between the 45,000-foot excursion and minimal dwell vs. 14,000-foot base line SpO_2 as a result of experimental time constraint. Therefore, incrementally decreasing oxygen flow rates were not obtained at the 45K'.

40,000 foot – Only one SpO_2 value was collected at this independent variable altitude due to an overabundance of caution and thus non-linear curve fitting was not performed.

35,000 foot – SPSS non-linear curve fitting was applied to data aligned in three columns: SubjectID, Oxygen_LPM, and SpO_2 (as dependent the variable). The model expression equation chosen: A / (1 + EXP(-B * (Oxygen_LPM - C))). Parameter estimates generated by SPSS were: A(97.708), B(2.777), C(-.020). These parameters were further adjusted via TRANSFORM to improve the accuracy of SpO_2 predicted values to equal experimental averages for a final equation: 97.71 / (1 + EXP(-2.78 * (Oxygen_LPM + .02))). The SpO_2 value 80.75% (OFOS average value for 14K' equivalence) was found to correspond to oxygen flow value of 0.54LPM at this 35,000-foot altitude. This non-linear curve-fitting procedure was repeated for the remaining experimental altitudes.

30K'; final equation = 98.7 / (1 + EXP(-3.1 * (Oxygen_LPM + 0.048))). SpO_2 80.88% (as close to 80.75% SpO2 as SPSS would generate) corresponded with an oxygen flow rate of 0.44LPM at 30K'.

25K'; Final equation: 98.8 / (1 + EXP(-3.3 * (Oxygen_LPM + 0.13))). SpO_2 81.04% corresponded with an oxygen flow rate of 0.33LPM at 25K'.

20K'; Final equation: 98.2 / (1 + EXP(-4.3 * (Oxygen_LPM + 0.2))). SpO_2 80.98% corresponded with an oxygen flow rate of 0.16LPM at 20K'.

18.5K'; Final equation: 98.2 / (1 + EXP(-4.6 * (Oxygen_LPM + 0.22))). SpO_2 81.2% corresponded with an oxygen flow rate of 0.12LPM at 18.5K'. Additionally, SpO_2 90.31% corresponded with 0.31LPM at 18.5K' thereby indicating equivalence with the 10,000 foot SpO_2 base line. Both values are included in curve "C" generation.

15,000 foot – SPSS; Analysis final equation: 96.5 / (1 + EXP(-6.36 * (Oxygen_LPM + 0.24))). SpO_2 90.26% corresponded with an oxygen flow rate of 0.18LPM at 15K'.

12,000 foot – SPSS; Analysis final equation: 94.36 / (1 + EXP(-7.6 * (Oxygen_LPM + 0.31))). SpO_2 90.35% corresponded with an oxygen flow rate of 0.10LPM at 12K'.

C-curves were generated with these calculated outputs per the procedure described in the SAE 8025A. Separate C-curves were generated for individual 10K' (Figure 3) and 14K' (Figure 4) base line comparisons.

Figure 3

Curve "C" Representing Oxygen Flow Rate in Liters per Minute Under Normal Temperature Pressure Dry (NTPD) Conditions Necessary to Maintain 10,000 Feet Equivalent Blood Oxygen Saturation Level Baseline as Experimentally Determined

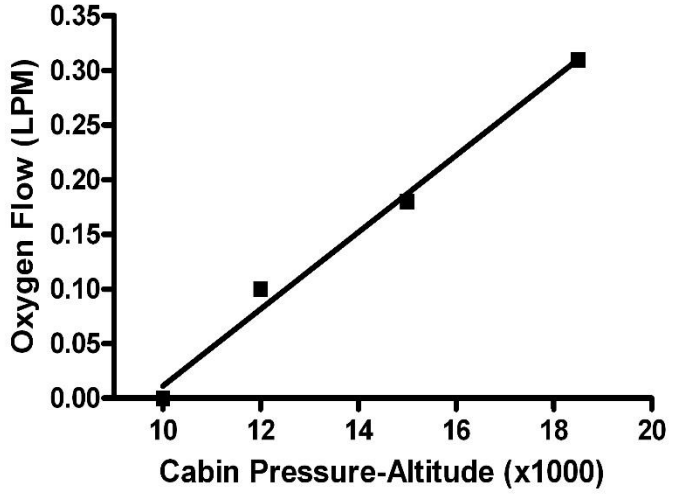
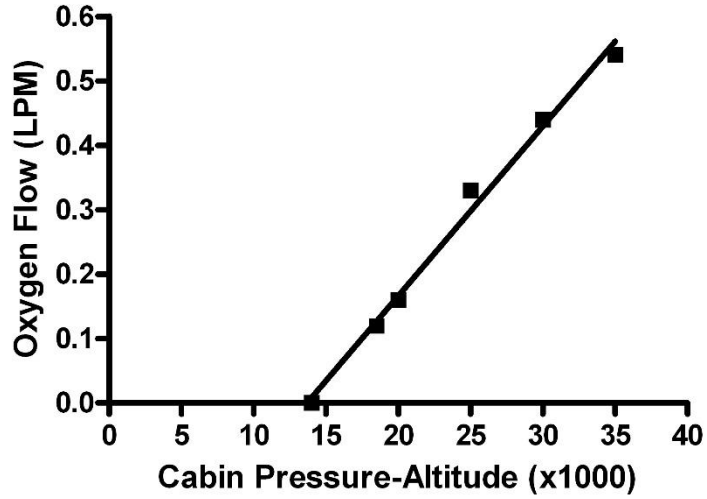


Figure 4

Curve "C" Representing Oxygen Flow Rate in Liters per Minute Under Normal Temperature Pressure Dry (NTPD) Conditions Necessary to Maintain 14,000 Feet Equivalent Blood Oxygen Saturation Level as Experimentally Determined



SpO_2 Data Collection Challenges

* Stable SpO_2 data was elusive unless the SpO_2 result was >97%. A period significantly greater than 3 minutes was necessary to allow 1-minute and 3-minute averages to align.

* Large breaths (i.e. yawns) that overbreathed the oxygen supply bag at high altitudes caused dips in the SpO_2 that recovered over time.

* Large breaths representing greater oxygen need than the oxygen bag supplied (ex. Subject 6, large male, lowest oxygen flow at 35k') caused low but true SpO_2.

* Large breaths at 18.5k' and lower will supply more oxygen to any given subject's biological system and therefore are reflected with significant SpO_2 rise. If larger breaths are maintained as greater respiration, then a higher sustained SpO_2 results and false high values of seemingly stable SpO_2 may be assumed.

- This happenstance represented the largest challenge to accurate data collection as 10k' and 14k' base line stable SpO_2 assessment relied upon normal tidal breathing with no interfering yawns, sighs, talking or movement while sitting. Additionally, human subjects tended to fall asleep in the 6th hour of research thereby causing momentary breath holds/large breaths to occur that perturbed SpO_2 readings. The effects of a single large breath resolved approximately 30 seconds to one minute.

A summary of this experience is to convey that there is no appropriate "time" that allows assessment of stable SpO_2, but rather great effort must be made by the PI and Subject to ensure accuracy with minimal interference and utmost focus upon methodology.

45,000' Gradual/Emergency Decompression Descriptive Analysis

Twelve human subjects wearing aviation passenger masks supplied with 3.24LPM oxygen were ascended at 6500 ft/min in the hypobaric chamber from 30,000' to approximately 44,800' and left to dwell for a target 10 to 20 seconds at peak altitude, then descended to 40,000' at 10,000 ft/min. Data are reported in Table 4. Associated SpO_2 values (average lowest SpO_2 at 45k' was 81.58%, recovery at 40k' stabilized at SpO_2 94.33%) are reported in Table 2.

Table 4

45,000' excursion data. Illustrated are the time above 40K' (avg. 98.0 seconds) & 44k' (avg. 34.8 seconds) and altitudes of respective SpO2 recovery (avg. 41128' and 40748'; rapidly dropping SpO2 was stabilized and began to climb, respectively)

	Subj1	Subj2	Subj3	Sub4	Subj5	Sub6	Subj7	Subj8	Subj9	Subj10	Subj11	Subj12	avg	sem
above 40k' (sec)	88	98	110	82	139	94	97	88	89	109	94	89	98.0	4.4
above 44k' (sec)	29	39	49	23	58	35	36	29	29	26	35	29	34.8	2.9
SpO2 trough (alt')	40095	41978	40113	42194	42048	40471	40219	40408	40353	43461	41933	40258	41128	326.0
SpO2 rising (alt')	40037	41398	40068	41124	40328	40283	40153	40383	40350	43435	41197	40222	40748	278.9

Respiratory Data – Descriptive Analysis

Participant individual and group average values for breathing rate (BPM; Table 5) and breathing total amount per minute (minute volume; Table 6) by altitude and decreasing oxygen flow are presented. Changes in breathing rate and minute volume were expected in response to a decompression event exposure.

As previously stated, prescribed respiration values (breathing rate and tidal volume) are listed in § 25.1443(c)(1) and (2) participant breathing instructions are provided in SAE AS8025A for passenger mask oxygen certification tests. SAE AS8025A standard assumes hyperventilation as presented in the Introduction section (p.2, paragraph 1), that the breathing machine per standard is to be set for 1.1 liters per breath tidal volume at 30 LPM minute volume. This study attempted to gather data to test that assumption via human respiratory response assessment. This question and answer pertains to the “Potential Beneficial Outcomes” section on p.1. Even though mask certification tests may favor the use of mechanical breathing simulators for ease of use and cost-savings, human empirical respiration data are necessary for input into breathing machine simulations.

In this study, the number of breaths per minute decreased at higher altitudes with diminishing oxygen flow rates. No change in breathing rate was noted between altitudes with PAX mask (standard) prescribed oxygen load. Base line values were tested in order of ground level, 10K’ and 14K’ SpO2 baseline altitudes, then the experimental flight altitudes and are illustrated as such. Average participant ground level breathing rates (in chamber/just before flight) were much higher than the normal average human breathing rate of 12-15 BPM due to lack of experimental control of each Subject, i.e.) talking, moving, etc.

Note: Reminder of methodology. Participant individual and group average breathing rate (BPM) data (Table 5) and breathing depth (minute volume) data (Table 6) are presented within an altitude level by decreasing oxygen flow rate from prescribed maximum flow rate at that altitude as stamped on mask, 75% of maximum flow rate, 50% of maximum flow rate, and 25% of maximum flow rate. At lower altitudes, a zero-flow rate of oxygen is substituted for the lowest flow rate and/or added.

Table 5 (with accompanying graph)

Participant Individual and Group Average Breathing Rate Values by Altitude and Decreasing Oxygen Flow Rate. Data are presented in the accompanying graph as group breaths per minute (mean + SEM) by altitude (K') and oxygen flow rated (LPM).

alt	O2 LPM	Subj1	Subj2	Subj3	Sub4	Subj5	Sub6	Subj7	Subj8	Subj9	Subj10	Subj11	Subj12	avg	sem
BL b4	ascent	26	23	20	31	35	23	26	18	24	30	23	15	24.5	1.6
10k'	BL	19	20	20	15	27	25	15	19	14	20	14	15	18.6	1.2
14k'	BL	20	21	15	19	23	13	19	16	19	23	13	13	17.8	1.1
45k'	3.24	18	30	10	22	20	14	18	18	23	24	21	19	19.8	1.5
40k'	3.10	19	32	17	19	28	17	17	16	20	20	14	19	19.8	1.5
35k'	2.55	14	23	19	22	17	13	21	21	21	23	15	20	19.1	1.0
	1.90	17	18	24	22	14	15	17	16	18	19	12	21	17.8	1.0
	1.28	15	14	15	24	28	13	16	21	17	20	11	14	17.3	1.4
	0.64	13	21	15	27	13	18	14	15	18	18	13	14	16.6	1.2
30k'	2.00	24	26	12	27	21	23	14	17	17	23	20	18	20.2	1.4
	1.50	18	20	18	28	21	16	15	15	18	19	15	13	18.0	1.1
	1.00	15	23	12	25	17	14	15	14	14	20	11	13	16.1	1.3
	0.50	15	16	10	20	10	17	15	19	18	19	12	13	15.3	1.0
25k'	1.50	19	25	11	29	27	21	21	23	19	21	15	17	20.7	1.5
	1.13	15	22	26	30	16	26	29	19	19	18	13	13	20.5	1.7
	0.75	13	14	14	28	17	23	15	15	18	21	12	14	17.0	1.4
	0.37	13	21	8	22	9	17	13	16	19	18	14	14	15.3	1.3
20k'	1.17	13	37	12	37	23	20	14	17	19	22	13	16	20.3	2.5
	0.88	16	26	12	26	14	19	14	19	18	22	12	15	17.8	1.4
	0.59	16	16	14	21	12	27	13	19	16	18	12	13	16.4	1.3
	0.30	17	36	16	21	9	20	13	16	18	20	13	15	17.8	1.9
	0.00												13	13.0	n/a
18.5k'	0.83	23	33	12	15	30	26	15	16	17	22	14	17	20.0	2.0
	0.62	21	30	13	23	22	23	12	18	18	17	12	14	18.6	1.6
	0.42	12	28	24	22	15	24	14	15	18	17	12	16	18.1	1.5
	0.21	19	36	15	28	15	18	14	15	21	17	11	15	18.7	2.0
	0.00							15	17	21	17	17	14	16.8	1.0
15k'	0.50	13	28	14	22	21	20	19	22	19	14	16	14	18.5	1.3
	0.38	17	20	32	19	16	18	16	21	18	19	16	15	18.9	1.3
	0.25	15	16	14	20	13	19	15	15	19	18	13	13	15.8	0.7
	0.13	15	19	15	25	17	15	15	18	18	20	14	16	17.3	0.9
	0.00							15	16	19	21	11	14	16.0	1.5
12k'	0.25	11	19	16	19	18	16	14	20	18	21	13	16	16.8	0.9
	0.19	16	15	25	21	16	23	14	22	18	18	13	15	18.0	1.1
	0.13	12	21	20	24	22	18	16	19	18	16	13	16	17.9	1.0
	0.00	12	18	19	21	18	20	13	17	19	18	13	13	16.8	0.9

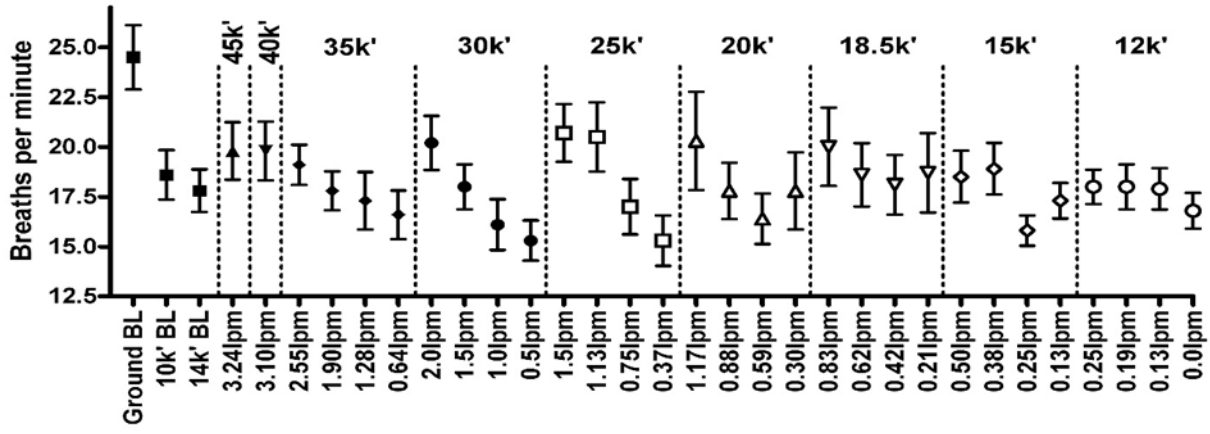


Table 6 (with accompanying graph)

Participant Individual and Group Average Breathing Depth Values by Altitude and Decreasing Oxygen Flow Rate. Data are presented in the accompanying graph as group breathing volume per minute (mean + SEM) by altitude (K') and oxygen flow rate (LPM)

alt	O2 LPM	Subj1	Subj2	Subj3	Sub4	Subj5	Sub6	Subj7	Subj8	Subj9	Subj10	Subj11	Subj12	avg	sem
BL b4 ascent		8177	6952	7734	11741	14364	11465	9256	10236	8461	8392	10538	7230	9546	621.5
10k' BL		8458	9153	9095	14230	11436	11187	8901	5117	5391	4221	9255	6157	8550	848.6
14k' BL		11698	7377	9102	11146	10043	8731	5786	6764	4549	4636	9002	5646	7873	615.7
45k'	3.24	10776	7739	7706	10061	15151	13402	9040	7518	7533	12496	13163	8696	10273	773.7
40k'	3.10	5195	5925	4512	7520	10070	10101	6678	7500	5291	6513	9596	4525	6952	570.2
35k'	2.55	4451	5626	4381	6883	9674	10534	6453	5981	5539	6696	11262	3080	6713	704.2
	1.90	4440	8596	3581	6088	8364	14702	5582	5916	5804	8447	9239	3271	7003	876.1
	1.28	5602	7717	6060	7508	5654	14229	6177	5104	5930	8469	10077	5322	7321	744.2
	0.64	6272	6746	11807	7078	9158	14525	6922	4700	8111	10043	10166	5800	8444	788.7
30k'	2.00	5281	6067	5974	6852	5149	7818	4646	4320	5227	7303	7461	3361	5788	394.2
	1.50	4728	5996	5159	3802	7102	11854	5546	5108	5704	8063	6329	4163	6130	610.1
	1.00	6015	7034	8635	6741	7909	12422	6033	5263	6000	9267	9964	5424	7559	609.1
	0.50	6134	8585	9156	6993	7719	19533	7751	7670	10418	9293	10492	5933	9140	1000.2
25k'	1.50	6243	4543	4465	4429	6718	8852	10009	5452	10161	8937	9509	3461	6898	710.2
	1.13	3732	6392	4370	4229	6236	10905	11046	4779	9612	7528	8272	5021	6844	699.8
	0.75	5339	8783	8974	4582	4967	10841	7506	5644	10364	8832	8928	5563	7527	606.8
	0.37	5466	8567	7569	5781	6806	21233	7325	5591	10964	9698	11407	6498	8909	1223.0
20k'	1.17	6746	4131	8335	5137	5450	13796	5053	6125	10486	5782	10838	5024	7242	861.6
	0.88	4108	7735	9090	3926	7444	16568	6855	3376	9580	8245	9427	5845	7683	967.7
	0.59	4174	6078	11140	6005	7510	18109	7200	5498	8984	7143	9375	4986	8017	1023.1
	0.30	7523	6623	10604	4957	8732	17782	6609	5855	10186	8310	10888	6677	8729	984.5
	0.00												7956	7956	n/a
18.5k'	0.83	6374	4119	10752	9764	5426	10222	3505	5690	9474	5816	7891	4113	6929	746.0
	0.62	10561	5292	11372	5467	5447	15355	4388	5766	9753	7059	9163	4539	7847	950.9
	0.42	7642	6530	9317	6054	7176	15983	5389	5892	9891	7281	9431	5976	8047	841.7
	0.21	5615	5694	11600	6572	7945	19731	7094	6839	11314	8208	11663	5787	9005	1136.7
	0.00							6713	8425	11078	8933	13329	6397	9146	916.4
15k'	0.50	5385	7846	9507	4643	5806	16198	4860	4691	10336	5996	7808	5251	7361	958.1
	0.38	6263	6803	4628	5821	5707	18098	4939	3603	11126	7901	9372	5978	7520	1127.4
	0.25	5670	6705	13089	6001	7316	14269	4955	4477	12209	7828	7895	5139	7963	948.2
	0.13	7342	7371	11964	7520	6202	21091	6670	6477	10636	8487	9595	6304	9138	1196.7
	0.00							6709	6968	11173	9191	10222	6286	8425	707.3
12k'	0.25	6205	6275	9169	6182	6486	15380	4871	4988	8902	6391	8203	5584	7386	824.5
	0.19	7474	7130	8974	7189	6201	12348	4689	4895	9529	7775	9478	4868	7546	658.8
	0.13	5892	6774	6423	5654	6379	10061	5311	7793	9928	6460	9220	4975	7073	499.9
	0.00	9212	8211	8196	6361	6772	16438	5374	7119	10132	8242	8435	4964	8288	855.9

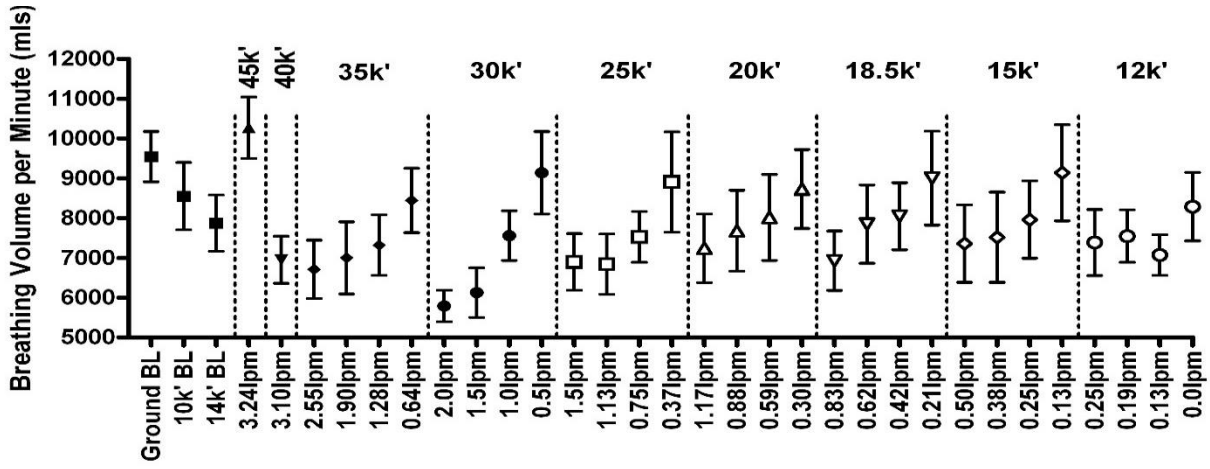
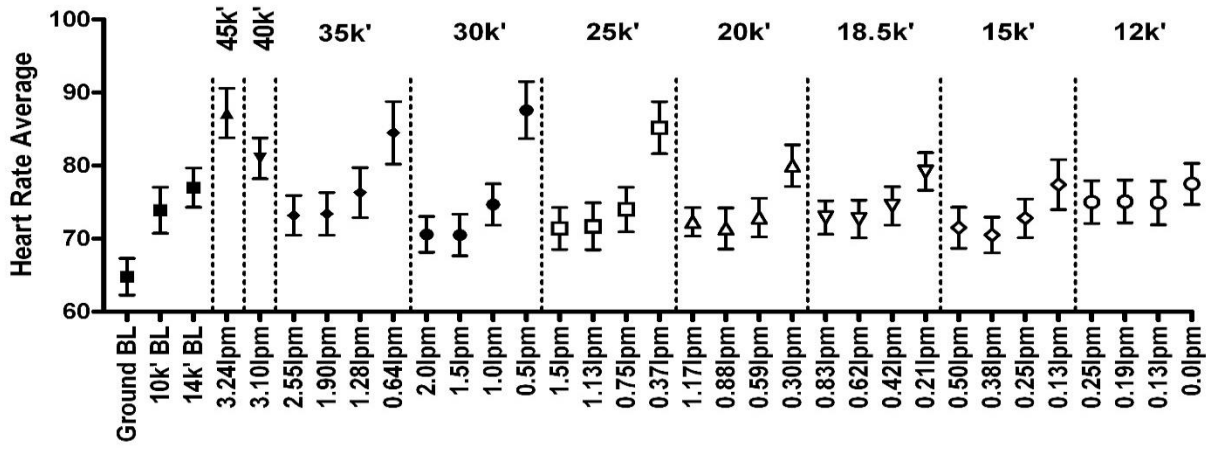


Table 7 (with accompanying graph)

Participant Individual and Group Average Heart Rate Values by Altitude and Decreasing Oxygen Flow Rate. Data are presented in the accompanying graph as group heart rate per minute (mean + SEM) by altitude (K') and oxygen flow rate (LPM)

alt	O2 flow	Subj1	Subj2	Subj3	Sub4	Subj5	Sub6	Subj7	Subj8	Subj9	Subj10	Subj11	Subj12	avg	sem
HeartRate rest		60	70	65	63	75	73	71	57	65	74	45	59	65	5.3
10k' BL		67	79	76	70	87	79	82	69	75	89	49	65	74	6.1
14k' BL		72	82	76	74	79	86	82	75	80	92	54	71	77	6.2
45k'	3.24	71	93	91	90	78	84	99	79	92	112	73	83	87	7.0
40k'	3.10	68	88	89	74	88	82	93	77	80	93	63	77	81	6.5
35k'	2.55	64	81	81	61	80	76	86	70	70	84	57	69	73	5.9
	1.90	64	82	82	63	81	80	86	70	70	82	55	67	73	5.9
	1.28	66	94	81	65	81	87	94	68	72	80	57	70	76	6.0
	0.64	68	110	90	74	84	109	94	69	72	89	69	85	84	6.6
30k'	2.00	66	78	78	61	68	70	82	67	75	82	55	67	71	5.7
	1.50	62	79	78	58	74	74	86	67	71	79	52	65	71	5.7
	1.00	65	88	76	73	80	83	87	70	71	80	53	71	75	5.9
	0.50	72	103	97	99	91	105	96	82	72	84	64	86	88	7.0
25k'	1.50	66	69	72	62	77	70	96	72	70	81	55	68	71	5.9
	1.13	64	73	71	61	76	79	98	70	72	78	53	66	72	6.0
	0.75	66	89	74	64	77	80	93	70	74	79	56	66	74	5.9
	0.37	72	104	87	84	89	100	99	77	77	89	62	83	85	6.7
20k'	1.17	67	74	73	67	76	78	85	70	71	79	60	68	72	5.8
	0.88	61	83	75	59	78	80	83	70	70	77	53	68	71	5.7
	0.59	60	77	76	70	76	84	86	69	74	78	54	70	73	5.9
	0.30	70	84	78	80	81	90	98	74	79	85	59	81	80	6.5
	0.00												104	104	n/a
18.5k'	0.83	65	73	75	71	75	77	83	71	77	83	53	71	73	5.9
	0.62	67	74	74	65	75	81	88	70	76	80	53	69	73	5.9
	0.42	68	80	75	73	77	89	83	72	77	81	54	67	75	6.0
	0.21	69	79	73	80	82	87	94	80	83	88	61	77	79	6.4
	0.00							110	90	100	97	70	93	93	10.8
15k'	0.50	60	82	68	74	74	82	84	72	68	76	50	69	72	5.7
	0.38	63	75	63	73	75	79	84	71	67	76	53	68	71	5.7
	0.25	62	78	70	74	76	78	87	73	70	83	53	70	73	5.9
	0.13	62	86	71	86	77	86	99	78	71	81	55	76	77	6.3
	0.00							105	86	86	88	57	87	85	9.8
12k'	0.25	63	85	68	72	72	87	87	74	86	78	55	72	75	6.0
	0.19	69	90	71	73	74	84	90	73	71	79	53	70	75	5.9
	0.13	69	90	68	71	72	81	93	75	71	83	56	71	75	5.9
	0.00	70	82	67	79	76	85	95	82	72	85	58	78	78	6.3



Heart Rate Data – Descriptive Analysis

Changes in heart rate (beats/minute; Table 7 above) are expected in response to research protocol exposure firstly due to white-coat syndrome or unfamiliarity with hypobaric chamber operations. Resting heart rates were collected while seated for at least 10 minutes in the PI's office, whereas the 10K' and 14K' base line and altitude/oxygen flow scenario associated heart rates were collected in the last minute of chamber flight of each scenario. A trend of increased heart rate from ground level to 10K' to 14K' was revealed as was equally the case with decreasing oxygen supply per altitude tested thereby suggesting the heart rate responses recorded were due to hypobaria/hypoxia rather than fight or flight response. Trends may be present that seem to correlate with decreases in SpO_2 values. Increases in heart rate may signify cardiovascular compensation that partially preserves SpO_2. Heart rate increases in this respect may offer additional support for a transition point from the minimally to moderately hypobaria/hypoxia challenged passenger. However, such small increases in heart rate are not a cause for concern and are not proposed in this OFOS protocol to be an indicator of distress that must be avoided.

Decompression Sickness/Decompression Illness

Although not a variable of interest in this study, altitude DCS was of great concern given the total flight time of approximately three hours, the extremely high peak altitude (45K'), and the total flight time above 18K' -- all risk factors for DCS. It was a significant achievement that neither participants nor IOs (some of whom flew repeatedly in the chamber), reported any signs/symptoms of DCS in-flight, immediately post-flight, nor within 24-hours post-flight. Significant effort was made in the experimental flight profile design and 100% oxygen pre-breathe + exercise protocol to minimize the risk of DCS (these preventative measures are more completely described in Appendices A3 through A6). Participants and IOs were visibly assessed by the PI and chamber support staff for cutis marmorata and monitored for signs/symptoms of DCS throughout the flight and during the one hour "clean time" post-flight before release and the end of a testing session. Participants and IOs were instructed to notify and report to a local hospital if any DCS signs/symptoms emerged within 24 hours post-flight.

Discussion

Our data demonstrate that in a representative cohort of the American flying public, **(1)** significantly higher stable human blood oxygenation levels are maintained through use of a phase-dilution passenger oxygen mask than is required by 14 CFR 25.1443(c)(2) regulation, **(2)** breathing rates may show minor decreasing trends per altitude and oxygen flow supplied while breathing volumes show minor increasing trends, yet neither appear to differ from base line values, **(3)** heart rate may be a good indicator of physiologic challenge as it rises when oxygen supply rates are lowered to ¼ of that stamped on the mask, and **(4)** a brief transit as a passenger to 45k' while breathing oxygen from a PAX mask is tolerable (SpO_2 does not fall below 14 CFR 25.1443(c)(2) regulation guidelines) given that the simulated emergency cabin decompression includes a "pilot" response to descend the aircraft that prevents greater than 34 seconds elapsed time above a 44k' pressure-altitude and drops to or below 41K' pressure-altitude for subsequent adequate blood oxygenation level SpO_2 recovery.

What is the benefit of phase-dilution masks?

Oxygen flow calculations for maintenance of tracheal partial pressure do not consider the biphasic breathing components of inhalation vs. exhalation. An effective doubling of oxygen supply is afforded through use of phase-dilution PAX masks (as compared to cannula use). This project's data shows very little SpO_2 drop, unaltered breathing patterns/volume and minimal heart rate rise as a result of Subjects being provided half of the provided oxygen prescribed as stamped on the PAX mask.

Are regulations based upon assumptions that are too conservative in nature?

Hypoxia from the clinical perspective becomes a concern at levels < 94% SpO_2 in the general population whereas < 88% SpO_2 is the lower bar to clear for those with pulmonary or cardiovascular pathology; specifically COPD, emphysema, chronic bronchitis, and cystic fibrosis.(Driscoll et al., 2017) However, hiking at altitude (summiting Mauna Loa; 4,200m or 13,780ft) drove SpO_2 to 72% in 6 of 6 subjects.(Netzer et al., 2017) In the context environmentally induced hypoxia such as the case with mountain climbing and aircraft emergency decompression, regulations that require oxygen supply to maintain 83.8 mmHg TPP (80.75% SpO_2 per this study) for passengers at all times may warrant deeper consideration for its conservative assumptions.

This study experienced only one communication difficulty with a human subject at 65% SpO_2. Tingles and paresthesia were reported by some between the 70-75% SpO_2 range, yet communication, compliance and behavior were never compromised in this subset. Although level of mental deficit was not tested, experimental success despite human subjects experiencing multiple bouts of hypoxia at the SpO_2 70-75% extent signify that a resting passenger is adequately supported by oxygen supply that result in less than 80.75% SpO_2.

Are there additional actions that further afford economy of oxygen delivery that remain safe?

Potentially yes there are additional actions. A key goal of this study convention was to provide support for facilitation of technological progress. The phase-dilution PAX mask provides an advantage in its method of oxygen collection during exhalation and increased concentration of oxygen in its users' alveolar space, yet its benefits are masked by the current regulatory tracheal partial pressure (TPP) focused assessment of adequate oxygen delivery.

Why conduct this research study in a hypobaric chamber rather than simple oxygen/nitrogen ratio reduction to simulate hypoxia?

In a study of only 6 human subjects, each was exposed to similar conditions: 1) mountain hike to 4,200m and 2) simulated hike on a treadmill under normobaric conditions with oxygen supply equivalent to 4,200m. Hypobaric hypoxia resulted in significantly lower SpO_2 than normobaric hypoxia conditions (80.2% vs. 85.8%; p=0.027).(Netzer et al., 2017) Passengers exposed to an aircraft cabin decompression experience a greater drop in SpO_2 than the equivalent normobaric oxygen decrease would induce. Other effects of hypocapnia and barometric influence on breathing rate/depth as well as heart rate occur differently or not at all in environments of hypoxic challenge alone. Furthermore, data collected in this OFOS project are now the gold-standard for gradual decompression effects that may then be compared with rapid decompressions in the future for which lesser mental acuity and faster rate to achieve unconsciousness is expected. OFOS research methodology sought to reproduce cabin decompression as accurately as possible.

What improvements could be made to this line of research? a.k.a. Study Limitation

Near infrared spectroscopy sensors were planned for placement on the forehead for cerebral StO_2 readings that may have been a most relevant location for correlation with cognitive ability or degradation during decompression exposure. Safety being the premier focus at 45,000 feet pressure-altitude, it was suspected that the military helmet and partially bayonet clipped oxygen mask would be beneficial to have on the ready for loss of consciousness and its presence was therefore implemented. Military helmets (in our possession) did not have built in NIRS sensors and interfered with adequate placement of OTS NIRS sensors and therefore this opportunity was lost. Finger SpO_2 is arguably a better indicator than alveolar oxygen partial pressure and undoubtedly a real-time indicator that is superior to human conditions calculated with tracheal partial pressure as defined by current regulations.

Conclusions/Recommendations

Primary scope - In summation, positive findings within the OFOS study indicate: 1) benefits would be realized from moving away from prescriptive-based standards to more physiologically relevant, performance-based standards such as the SpO_2 variable of this study's focus to better describe aircraft passenger safety in addition to providing an easier template for oxygen systems manufacturers in which to abide and 2) re-evaluation of oxygen flow (L/min) volumes necessary to maintain passengers' blood oxygen saturation levels is warranted. These research data and analyses add to the collective scientifically founded momentum to justify a rule-making session that favors use of empirical physiological data independent variables, such as are employed in the OFOS protocol, in lieu of engineering/mechanistic/computer science calculations of oxygen supply adequacy that are currently used and required by FAA doctrine.

Secondary scope - Passenger travel above 40,000' was investigated via transit of human subjects in the hypobaric chamber to 45,000' while breathing oxygen at 3.24LPM. As aircraft that fly at this altitude with fan blade/engine placement aft of the bulkhead greatly diminish the risk of rapid decompression events, the parameters tested in this study of gradual decompression elucidate a phenomenon of adequate passenger oxygenation if the pilot descends the aircraft within 17 seconds. This is an exceedingly unlikely event as cabin pressure-altitude in most regulations are capped at 40,000 ft. Interim policy (Reference Amendment 25-87) memo ANM-03-112-16 describes how the FAA evaluates the petitions for exemptions to § 25.841(a) following certain failures which may result in a cabin pressure-altitude above 40,000 for a maximum total exposure time of 1 minute. The OFOS 45,000' excursion dwelled above 40K' for an average of 98 seconds (1 minute & 38 seconds), a scenario that exceeds regulatory time limit by over 50% while resulting in average human blood oxygen level (SpO2) not less than the 14 CFR 25.1443 specified low limit of 14K' equivalence.

Benefits specified in primary and secondary scope promote 1) less weight carried on each flight due to less oxygen candle weight needed, and 2) higher altitude flight that aids in decongesting airspace/ greater turbine efficiency. Improvements, if realized through modified regulations, will result in less fuel consumption, less operating costs, equivalent human oxygenation safety and greater flight safety with more options for flight level operations.

Additional specific recommendations:

1) During recovery from the emergency decompression scenario (descent from altitude/emergency descent), OFOS data showed arrest of decreasing SpO_2 at an average 81.58% and an average pressure-altitude level of 41,128'. Therefore, with pure focus upon oxygen supply at pressure-altitude, this indicates that passengers are adequately provided with oxygen per CFR regulation at approximately 41K' in an unpressurized cabin through use of the PAX mask and 100% oxygen of 3.24LPM flow. Positive pressure or extreme limitation of time exposure should be a primary factor if passengers are to be exposed to pressure-altitudes greater than 41K' by regulation or standard.
2) With time parameters of focus upon emergency decompression scenarios that should easily be resolved in 10 minutes' time, regulations would be simplified and adequate to

require 14,000’ pressure-altitude SpO2 equivalence for passenger needs. According to FAA regulations, oxygen supplementation of 10,000-foot SpO2 equivalence is required for passengers below 18,500 ft pressure-altitude by the same regulation that requires a 14,000-foot SpO_2 equivalence at altitudes above 18,500 ft. Reasoning that supports this requirement cannot be found and physiology subject matter experts cannot deduce reasoning in teleological fashion given the promoted discrepancy for oxygen needs. OFOS human subjects were kept at 14,000’ pressure-altitude for 10 minutes with no issues.

3) Interpretation of OFOS data must be applied to passengers, not aircrew. OFOS data only sheds light on adequate oxygen supply to those whose resting metabolic rate needs are being met and cannot be directly applied to flight attendants with any degree of workload or pilots with higher mentation and performance demands.

4) Interpretation of OFOS data must be applied with appreciation for the difference between rapid decompression and the gradual decompression simulated in this study. Rapid decompression to 45K’ (3 to 10 seconds) will undoubtedly result in a majority of passengers going unconscious due to the time needed for nitrogen washout of the lungs/impossibility of immediate 100% oxygen delivery. Those that don PAX masks before passing out will be adequately supplied oxygen with the delivery rates specified by OFOS. Those that are incapable of donning a PAX mask before passing out at 45K’ will experience extreme hypoxia for which duration over 7 minutes above 37K’ has been shown to cause brain damage that may eventually result in death.(Brierley & Nicholson, 1973) Therefore, the recommendation is to weigh severity of outcome appropriately with risk of event (rapid/explosive decompression vs. gradual decompression).

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SAE International Aerospace Standard (AS) 8025A Passenger Oxygen Mask, copyright protected document

FAA interim memo ANM-03-112-16, *Interim Policy on High Altitude Cabin Decompression,* AIR-620: Technical Innovation Policy Branch, https://drs.faa.gov/search and enter ANM-03-112-16 in search bar (accessed 09/23/2025)

Appendix A1. Health History Questionnaire

Completed by each participant, presented for PI/medical monitor prior to enrollment

Subject ID#: _____ Age (18 to 50): _____

Height (in): _____ Weight (lbs): _____

nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm BMI = _____

Circle one – 1st class medical/ 2nd class medical/ 3rd class medical/ no current medical

Flight time (hrs/wk total & if pressurized) _____

Exercise regimen hrs/wk, type_____

Are you able to run continuously for 20 minutes? Y / N Avg. pace? _____minutes/mile

Diver? (hrs/wk, depth, most recent dive) _____

Do you currently use tobacco? Y / N Type: _____ Frequency: _____

Have you ever smoked/vaped? Y / N Quit when? _____ How long/how regularly? _____

Any medical/clinical respiratory condition (e.g., asthma, chronic obstructive pulmonary disease [COPD], etc.) Lung injury/breathing illness? Y / N When_____ What_____

Do you have a history of or now have peripheral vascular/neuromuscular disease, neuropathy (stroke/epilepsy), high blood pressure, or Raynaud's syndrome? Y / N

Medical or physical limitations that would preclude a decompressive experience? Y / N

Have you, in the past or at present, experienced discomfort in confined spaces? Y / N

Have you donated blood, platelets or plasma in the past 30 days or have a known anemia? Y / N

Do you have any of the following: respiratory ailments such as asthma or emphysema; pregnancy; hypo/hypertension; diagnosed heart problems; chest pains, difficulty breathing; serious bodily disability, deformity, or dismemberment; spells of severe dizziness; diabetes requiring medication; claustrophobia; recent surgery; or any other chronic disease? Circle 1

Any chronic medical condition not listed previously? _____

Taking prescribed medications? Y / N Amount/type/reason:

Use nutrition/herbal supplement? Y / N Amount/type/reason:

Use otc medication (e.g., Tylenol/Advil) routinely? Y / N Amount/type/reason:

Sensitive to other's touch or uncomfortable in enclosed environments? Y / N

Please list any other comments regarding your medical history that might affect your ability to participate in this protocol.

Appendix A2. PRE-flight Subject Exam and Instructions

Completed morning of Subject experimentation after informed consent for confirmation of Subject qualification to participate

Subject ID #: _____ Age (18 to 50): _____

Four (4) Days Before Chamber Flight

1) Review informed consent and OFOS protocol documents

2) Avoid gas-producing foods (beans, spicy foods, etc.) for at least 3 days prior to experimentation. Each Subject knows his/her own gastrointestinal fortitude – Do not exceed. If you do exceed, then report and postpone. Let someone else attend that day.

3) Limit alcohol for 3 days prior to chamber flight. Dehydration will undoubtedly occur. Do not further contribute to this impending dehydration.

4) No self-medication for flu, cold, etc. If you become ill, please inform the contract company (employer), that will in turn notify the government immediately upon discovery of symptoms.

5) No diving for 72 hours prior to hypobaric chamber exposure.

6) Get a good night's rest prior to participation.

7) Limit cardiovascular exercise for 12 hours prior, resistance training 4 days prior and do not perform exercise that is not part of your regular routine for 2 weeks prior.

8) Begin to ween yourself off caffeine at least one week prior to participation.

DAY OF CHAMBER FLIGHT (checklist)

1) Once again, no self-medication for flu, cold, etc. If you become ill, please inform your employer immediately upon discovery of symptoms.

2) No or very low caffeine intake as it is a vasoconstrictor and dehydrating agent. If a headache is expected with no consumption, then take as little as possible to avoid a headache.

3) Eat a breakfast low in fats and protein. Cereal, pancakes, waffles, toast are suggested with no butter or syrup. High triglyceride (fats) blood levels are known to interfere with hematocrit tests. Sorbitol, fructose, raffinose (carbohydrate found in beans) all increase the incidence of gas production, so please try to avoid.

4) Avoid exercise that is not protocol related.

5) Use the restroom before entering hypobaric chamber. This will limit experimentation interruptions to use the urinal/potty in the hypobaric chamber.

6) Wear comfortable clothing. Females are suggested to wear a sports bra. Sensor placement may demand optimal access to skin on the upper torso.

7) Wear comfortable tennis shoes that do not stink. Shower using deodorant soap to wash every square inch of your body before arrival. You will be in a confined space. Respect others and save yourself the hours of discomfort.

8) BE ON TIME, please!

9) Reiteration - if you must cancel for any reason, please spread the word immediately to your employer. Many people prepare for one Subject's participation. Notification 24 hours prior or sooner is requested.

Physical Qualification/Inclusion Criteria

Hct (≥12.0g/dl): _____ Hgb (≥ 37%): _____ SpO_2 (> 94): _____% rest HR: _____ bpm

Resp: _____/min Temperature (< 100.0) : ____deg F

Height: _____" Weight: _____ lbs. BMI (≤ 40): _____

Present your 3rd class or greater medical certificate for record of validity and non-expired status. GTG Y / N

Non-smoker/non-vaper? Y / N

History of injury (sports, hobby, accident)?

Location _____ Pain level _____ Frequency _____

Location _____ Pain level _____ Frequency _____

Location _____ Pain level _____ Frequency _____

Exclusion Criteria review (all "NO" answers get a pass on the day of experimentation)

Facial hair? Y / N

Any cold, acute upper respiratory infection (URI), or respiratory issue within two (2) weeks prior to study participation Y / N

Not able to exercise at the marathon pace level for 15 minutes? Y / N

Personal items with you? Y / N

Currently taking any medication or drug which may impair physical or cognitive activity, or which precludes the operation of heavy machinery/driving? Y / N

Additional questions

Have you taken any medications/caffeine/alcohol within 24 hrs prior? Y / N

Amount and Type: Reason:

Recent illness? Y / N Symptoms/Severity 1-5/days? _____Recover Y/N

# of hours slept last night. _____ Do you feel well rested/was sleep sufficient? Y/ N

Appendix A3. Minimization of Decompression Illness Risk (Pre-Breathe with Exercise Protocol)

Test participants and Inside Observers (IOs) will undergo a pre-breathe protocol that incorporates controlled/timed exercise and 100% oxygen prior to maximum test flight altitude to decrease the risk of altitude decompression sickness (DCS). This procedural pre-breathe has been deemed acceptable by NASA to precede astronaut spacewalks/ extravehicular activities (EVA) and is called the Cycle Ergometer with Vibration Isolation System (CEVIS) Pre-Breathe Reduction Program (PRP) Expt4 Phase II protocol. CEVIS was designed to precede exposure up to 4 hours of 4.3 psia exposure (30,000 ft pressure-altitude) with 15 minutes of spacesuit 3.5 psia during spacewalk/EVA (35,000 ft pressure-altitude). NASA pre-breathe protocols significantly reduce the risk of Type I DCS (CEVIS calculated risk < 0.1%) and none have resulted in documented Type II DCS events in 2,188 astronaut spacewalk/EVA exposures. Additionally, in 244 tests with 7,692 exercising subjects, **neurological DCS is not observed until incidence of Type I DCS exceeds 15**%.(Gernhardt & R.D., 2000)

Previous FAA scientist, Robert Garner, produced a report in 1996 following experimentation using a similar flight profile to the OFOS protocol beginning with up to a 10-minute 40,000 foot excursion following a 2-hour 100% pre-breathe preparation without exercise. DCS was successfully avoided in this study.(Garner, 1996) Dr. Garner alluded to a belief, reasonable at the time but now antiquated, that flights over 18K' should be no longer than 1 hour. Additional research since 1996 revealed the safe ability to dwell at pressure altitudes of 30K' for 4 hours given appropriate pre-breathe protocol implementation.(Gernhardt & R.D., 2000; Webb et al., 2002)

The OFOS protocol goes far above and beyond in terms of development and risk-mitigation than Dr. Garner's research or any research reported in ADRAC testing, using a CEVIS protocol that is a 2.5 hour 100% pre-breathe using specific exercise of heavy and light order magnitude followed by non-ambulatory decompression exposure (sitting).

An Altitude Decompression Sickness Risk Assessment Computer (ADRAC) model was generated by the Air Force using empirical data from approximately 3,000 individual human altitude exposures to various altitudes with/without pre-breathe preparation. However, ADRAC does not estimate DCS risk above 40,000 ft and cannot consider the CEVIS pre-breathe with compound exercise risk of DCS minimization measures input (due to lack of entry of data into the computer model above 40,000 ft or regarding CEVIS pre-treatment).

Using ADRAC, by comparative analysis a 4-hour 100% oxygen pre-breathe alone provides protection of predicted 28% DCS risk if Subjects are exposed to 30,000 ft pressure-altitude for 4 hours. The CEVIS protocol using only 2.5-hours of 100% oxygen pre-breathe time plus selective exercise yields ZERO % DCS risk at the same altitude and exposure time – 30,000 ft for 4 hours. It should be noted that 28% risk of DCS occurs at 120 minutes at 40,000 ft following a 4-hour 100% oxygen pre-breathe with no exercise thereby implying that CEVIS may also render that specific exposure to have zero % incidence of DCS. However, that has yet to be empirically tested.

It must be noted that the risk being discussed in this protocol is for joint pain, pins & needles and in very rare cases, skin mottling, all of which are considered mild manifestations following US Navy medical definitions [Howle(Howle et al., 2017) and personal communication, Murray CA](Van Liew & Flynn, 2005) and do not require application of hyperbaric treatment tables with the exception of skin mottling preceded by moderate to intense itching. Type 1 DCS is not life-threatening yet is highly controlled against in this study. An account of expected outcomes (if DCS signs/symptoms occur during OFOS studies) can be reviewed in the NASA report "Description of 103 Cases of Hypobaric Sickness from NASA-sponsored Research (1982-1999)"(Conkin) and is illustrated the excel spreadsheet appended that isolates all participant data utilized to build ADRAC for two separate conditions that incorporate oxygen pre-breathe before altitude exposure: 1) those with a 135 minute 100% oxygen pre-breathe that were subsequently ascended to 29,500 ft (4 hours) or 2) or underwent a 120-minute 100% oxygen pre-breathe followed by 35,000 ft (30 minutes). Subjects either performed rope pull exercises or rested. Of those Subjects that presented with DCS at altitude (predominantly of the exercising at altitude group), a vast majority were sign and **symptom-free upon return to ground level** simply due to the recompression to original pressure.(Muehlberger et al., 2004) A 120-minute 100% ground level oxygen treatment was given regardless of resolution of DCS indicators. On this note, a NASA Engineering and Safety Center Technical Assessment Report (NESC-RP-10-00659) states, "The Review Committee recognizes that, based on its experience, Type I or —pain only bends goes away with simple repressurization with or without the respiration of O2. **Were it not to respond to repressurization it would not endanger the life of an astronaut even though it might affect operations**. If serious DCS were to occur during EVA, then the most probable mechanism would be via arterialization of venous gas emboli. This is because appropriate O2 pre-breathe would eliminate N2 from well-perfused tissues so that supersaturation would be highly unlikely and thus autochthonous bubble formation in the brain or spinal cord could not occur during EVA."(Brady, 2011)

The philosophy of the OFOS testing as focused upon safety and acceptable risk is more conservative than the 2019 NASA "Suited Ground Vacuum Chamber Testing Decompression Sickness Tiger Team Report" experimental parameters:

1. Zero predicted incidents of Type II DCS at 0.95 probability across all planned suited vacuum chamber runs between 2018-2028.
2. Less than 1/1000 (0.1%) predicted risk of Type II (serious) DCS for any single suited vacuum chamber run.
3. Less than 20% risk of Type I DCS for any single suited vacuum chamber run.

World War II necessitated high-altitude bombing and the advent of the jet engine put aviators at uncalculated risk of DCS, hypoxia and hypothermia until environmental controls of pressurization and heating/air-conditioning could be implemented. Research in the mid-1940s to 1960s established that the degree of depressurization (altitude attained), dwell time, and metabolic load at altitude all increased the risk of DCS Types I and II that are linked to deleterious reactions in the cardiovascular and nervous systems. "Never again will such provocative testing be performed and "modelers" of DCS must be content with these data to

define the upper range of dose-response curves."(Conkin, June 9, 2016) The OFOS project does not reproduce these conditions. Data gained from long ago research that deliberately promoted DCS Types I and II have been extensively considered to assure OFOS flight profile safety. The OFOS project seeks to describe appropriate oxygenation of airline passengers and therefore seeks to preserve Subjects in a non-DCS state for mission success, not due to concern for safety. As there is never an absolute 0% probabilistic computation of DCS risk, on the unlikely event that DCS Type II does occur to any Inside Observer or Subject, immediate safety will be assured with a trip to the hyperbaric chamber for treatment. Subsequently, the 45,000 ft pressure-altitude will be eliminated from the flight profile upon such an occurrence. One can consider a DCS Type II event as a result of OFOS testing to therefore be anticipated, intercepted with maximal effort, yet impossible to fully prevent. DCS Type I and/or Type II are simply experimental stop signs that indicate that it is time to remove the Subject or Inside Observer from the conditions that are promoting DCS. This removal will occur immediately, faster than any mission-related flight or return to surface from diving countermeasure can conceivably occur. Simple removal from said conditions has been shown repeatedly and veritably to resolve signs/symptoms of Type I DCS.

Appendix A4. Research Hypobaric Chamber Flights

Decompression Illness: Signs/Symptoms

Med Deck Operator/Supervisor and Assistant Med Deck Operator/Supervisor should and will be aware and look for the following as Inside Observers should and will be aware, able to spot these signs/symptoms and are hereby reminded to continuously look for DCS Type I signs/symptoms such as:

(1) Most Common - Musculoskeletal pain, especially in the joints such as the knees, elbows, shoulders, etc.

(2) Tingling in any extremity (i.e., arms, fingers, legs, etc.)

(3) Localized pain in armpits, groin, behind ears

(4) Swelling in any anatomical location

(5) Marbling of skin (cutis marmorata)

(6) Skin irritation (i.e., itchiness), skin rash, followed by marbling of skin

(a) Per US Diving Manual Rev 7 - **Cutaneous (Skin) Symptoms.** The most common skin manifestation of decompression sickness is itching. Itching by itself is generally transient and does not require recompression. Faint skin rashes may be present in conjunction with itching. These rashes also are transient and do not require recompression. Mottling or marbling of the skin, known as cutis marmorata (marbling), may precede a symptom of serious decompression sickness and shall be treated by recompression as Type II decompression sickness. This condition starts as intense itching, progresses to redness, and then gives way to a patchy, dark-bluish discoloration of the skin. The skin may feel thickened. In some cases the rash may be raised.

(7) Sudden extreme fatigue

(8) Difficulty in thinking – Not to be confused with insufficient oxygen, check mask fit and oxygen delivery

(9) Vertigo

(10) Nausea and/or vomiting

(11) Hearing abnormalities – Not to be confused with high altitude induced sound quality alteration

(12) Bloody sputum

(13) Loss of control of bodily function

(14) Tremors

(15) Loss of coordination

(16) Numbness – complete loss of feeling

Larger Categories of DCS Type II:

(1) US Navy Diving Manual 17-4.4.1 **Neurological Symptoms.** These symptoms may be the result of involvement of any level of the nervous system. Numbness, paresthesias (a tingling, pricking, creeping, “pins and needles,” or “electric” sensation on the skin), decreased sensation to touch, muscle weakness, paralysis, mental status changes, or motor performance alterations are the most common symptoms. Disturbances of higher brain function may result in personality changes, amnesia, bizarre behavior, lightheadedness, lack of coordination, and tremors. Lower spinal cord involvement can cause disruption of urinary function. Some of these signs may be subtle and can be overlooked or dismissed by the stricken diver as being of no consequence. The occurrence of any neurological symptom after a dive is abnormal and should be considered a symptom of Type II decompression sickness or arterial gas embolism, unless another specific cause can be found. Normal fatigue is not uncommon after long dives and, by itself, is not usually treated as decompression sickness. If the fatigue is unusually severe, a complete neurological examination is indicated to ensure there is no other neurological involvement.

(2) US Navy Diving Manual 17-4.4.2 **Inner Ear Symptoms (“Staggers”).** The symptoms of inner ear decompression sickness include: tinnitus (ringing in the ears), hearing loss, vertigo, dizziness, nausea, and vomiting. Inner ear decompression sickness has occurred most often in helium-oxygen diving and during decompression when the diver switched from breathing helium-oxygen to air. Inner ear decompression sickness should be differentiated from inner ear barotrauma, since the treatments are different. The “Staggers” has been used as another name for inner ear decompression sickness because of the afflicted diver’s difficulty in walking due to vestibular system dysfunction. However, symptoms of imbalance may also be due to neurological decompression sickness involving the cerebellum. Typically, rapid involuntary eye movement (nystagmus) is not present in cerebellar decompression sickness.

(3) US Navy Diving Manual 17-4.4.3 **Cardiopulmonary Symptoms (“Chokes”).** If profuse intravascular bubbling occurs, symptoms of chokes may develop due to congestion of the lung circulation. Chokes may start as chest pain aggravated by inspiration and/or as an irritating cough. Increased breathing rate is usually observed. Symptoms of increasing lung congestion may progress to complete circulatory collapse, loss of consciousness, and death if recompression is not instituted immediately. Careful examination for signs of pneumothorax should be performed on patients presenting with shortness of breath. Recompression is not indicated for pneumothorax if no other signs of DCS or arterial gas emboli are present.

Potential for DCS Associated Pain

Intermittent (Transient) pain is defined as mild to moderate pain (severity 1-4) for less than 60 seconds each occurrence. If these intermittent pains recur at or below 30K' for **5 min (maximum, once recognized/described by the subject as pain)** from their first occurrence, the exposure will be terminated. Typically, transient pains do not last that long and do not require termination. If the pain severity exceeds 4 or any pain above 30K', the exposure will be terminated immediately regardless of intermittent or constant nature.

Rationale: Pain can result from muscle strain and other factors and it may take some time to determine if the pain is due to DCS or the various exercises and body positional factors. Pre-flight Subject injury history may be taken into account as the pain experienced may be pre-existing. Regardless, anyone at any time can terminate the exposure for reasons of DCS signs/symptoms. Subjects and/or Principal Investigator can terminate experimentation for any or no specified reason.

Constant pain is defined as any pain lasting more than 10 seconds **once recognized/described by the Subject as pain**.

Rationale: Once a constant pain has been identified and communicated, the test termination criterion has been met and there is no reason to continue the exposure.

Pain Scale Severity

0 No pain

1-2 Mild

3-4 Moderate

5-7 Strong

8-9 Severe

10 Strongest imaginable

Appendix A5. Cycle Ergometer Vibration Isolation System (CEVIS) Procedure as occurs within the 100% Pre-Breathe with Exercise DCS risk-mitigation strategy

Early U2 military jet operations were plagued with incidents of DCS with a 1996 report revealing via pilot survey that 75% thought they had experienced DCS with 4.2% of flights involving symptoms, some of which were neurologic in nature.(Webb, 2010) Testing and evaluation occurred in 1999 at Beale AFB incorporating a dual-cycle ergometer using a quantifiable level of exercise for arms and legs in addition to the 100% pre-breathe protocol to reduce DCS in U2 pilots (called EDP [exercise during prebreathe]). The intensity of the exercise was designed to be sub-maximal to avoid fatigue that would potentially affect the subsequent flight mission. Results were promising (pre-breathe alone 2/7 DCS cases vs. EDP 0/97 DCS) yet implementation was left to the Commanding Officer's discretion. This EDP protocol is somewhat interchangeably termed with CEVIS yet has not been as fully developed as CEVIS phase II within NASA DCS-mitigation studies and procedures. The OFOS project incorporated CEVIS phase II as it is the current premier DCS intervention that has been published, peer-reviewed and well established.

Furthermore, the decompression that exists within in the CEVIS protocol as described/illustrated was endured by necessity rather than programmed for optimization. A requirement to breathe ambient atmosphere for a period of 15 to 90 minutes during the Hard Upper Torso (HUT) donning procedure in the crewlock was a significant operational constraint for NASA on pre-breathe design. "To mitigate the adverse impact of this air breathing break, the Extra Vehicular Activity (EVA) crew completed the donning procedure for the Lower Torso Assembly of the Shuttle EMU in the crewlock while being slowly decompressed to 9.6 psia. The crewlock was then backfilled with oxygen to bring the crewlock to a pressure of 10.2 psia with the maximum allows FO2 of 26.5%, after which the crew breathed ambient atmosphere to complete the HUT donning procedure. 100% oxygen breathing was resumed with recompression of the crewlock to cabin pressure as soon as it became possible and before final decompression to EMU pressure and egress for EVA."(Gerth, 2018) Therefore, in the interest of minimizing DCS risk during OFOS experimentation, this decompression excursion was removed from the pre-breathe protocol whereas exercise and all other aspects remained

<u>Hypobaric Chamber procedure/CEVIS Pre-Breathe portion</u>:

1) Following ear pressure clearing check and 10,000ft/14,000 ft pressure-altitude base line chamber flight, Subjects and Inside Observers will don aviator masks that are tethered to the chamber oxygen supply systems and 100% oxygen will be delivered.
    a. IOs will assess mask fit and oxygen delivery. Mask leak must not be allowed to occur during pre-breathe and ascent to 30,000'.
    b. Upon IO all clear for transition to pre-breathe procedure, Subject will mount Rogue Fitness Echo Bike provided.
2) AM-400 Chamber Control or the Principal Investigator starts the 100% pre-breathe mission clock that will indicate completion of procedure when 150 minutes (2.5 hours) has elapsed.

3) Polar watches will be pre-loaded with individuals' anthropometric data and will already be on each chamber occupant's wrist. Heart rate (HR) zones will be indicated on the Polar watch. HR will also be visible on the Echo Bike display and is tracked/recorded on the master computer LabVIEW program.

4) On the Principal Investigator's request and IOs concurrence that Subject is ready/GTG, Subject will begin exercising with intentional performance and VERY minimal effort at this point as familiarity and comfort are important at the outset of exercise (100% oxygen mask donned and adjusted on face for max comfort):

    a. Leg exercise – rotational in nature. Deliberately move legs in circular fashion. Rather than pushing down alone, leg muscles should be used with all motions of the cycle phase in mind. Think about and perform moving each leg forward, down, back, and up (yes, avoid having the pedal push the foot/leg up but provide as little resistance to pedal elevation as possible without lifting the foot off the pedal).

    b. Arm exercise – push/pull in nature. Focus upon both pushing and pulling at the optimal time. Do NOT allow elbows to lock/always maintain a bend at the elbow even at full extension (seat is adjustable forward and aft to assure this reality).

5) The Subject will exercise for 10 seconds at an easy pace (50 to 100w). Comfort will be assessed. IOs will adjust bike seat post higher/lower and forward/aft for optimal positioning. Subject will again exercise for 10 seconds/readjust.

6) Upon GTG acknowledgement by IO following discussion and adjustments with Subject and other IO, all will mount an Echo Bike and exercise will begin:

    a. Principal Investigator inputs age into LabVIEW program and max HR is estimated using the 220 minus age equation. The LabVIEW program captures HR and indicates if at least a 77% max HR (unique to each participant and IO) has been established for which a green light and timer were activated. If the participant's HR fell below 77% max HR, then the timer would stop and await achievement of 77% HR max again before restarting. Inside Observers and Subjects must equal 85% max HR at some time to assure no chronotropic insufficiency is present, indicative of higher risk of future cardiac events and potential for ischemia.(Lauer et al., 1999)

    b. Inside Observers will be familiar with the procedure and maintain a 77-85% max HR as indicated on the Polar watch with supplemental indicators coming from the Echo Bike display (approx. 166 Watts) and guidance from PI,

    c. Subjects will attempt to maintain 77-85% HR_{max} via Polar watch feedback, yet will also be tracked by the medical deck (PI) and given inputs to increase/decrease/ maintain level of effort and for what duration. A Webb report opined that 75% HRmax was adequate for the pre-breathe protocol.(Webb, 2010) The Swain equation equates 75% VO2max to an 85% HR_{max} for which effort is said to be equivalent to a marathon running pace that is therefore sustainable for hours.(Swain et al., 1998)

* Effort necessary as gleaned from the literature (Astrand P.O. Rodahl, 2003; Gerth, 2018) establishes an expectation of a constant Watt output production (I_{ex} – 2.36 L/min; 167.44 Watts; 708.8 kcal/hr; 33.8 mL O_2/kg*min; 75% $\dot{V}O_{2\ max}$) as will be indicated (approx. 170 Watts) on the exercise bike display if appropriate effort is expended. This is an expectation of level of effort, yet HR will be the primary data point followed and adjusted as stated in 6a) and 6b) above. **Target HR and duration is: 77-85% HR_{max} (individually assessed) and 10 minutes <u>in zone</u>**.

* Warm-up time is not counted for time in 85% HR_{max} zone.

7) Conclusion of vigorous exercise is estimated to fall between 15 and 20 minutes into the pre-breathe protocol. At this time, all will remain seated on the Echo bikes.
8) 5 minutes post-exercise, all will dismount the bikes, towel off if necessary, drink water, take a seat.
    a. Rest for approximately 35 minutes

---

55 total minutes have elapsed in the pre-breathe protocol at this time

9) Begin Lower Torso Assembly (LTA) donning simulation. Light exercise during CEVIS PRP phase II has been estimated (I_{ex} = 0.41 oxygen L/min; 8.81 Watts; 121.8 kcal/hr; 5.8 mL O2/kg*min; 12.9% $\dot{V}O_{2\ max}$). For comparison, resting is I_{ex} = 0.305 oxygen L/min and zero Watts. Light exercise is therefore slightly exertion above resting and will therefore be simulated with stretching. One cycle of stretching interspersed with minimal exertion will be performed 4 times at 55-, 65-, 75- and 85-minute timepoints. Perform each stretch for 10 seconds:
    a. Sit on the floor and reach for the ceiling
    b. Transition to touching or reaching for your toes
    c. Point your toes to one wall and reach for the opposite wall
    d. Step back with your left leg, touch your left knee to the ground
    e. Stand back up, step back with your right leg, touch your right knee to the ground
    f. Stand back up, back scratcher shoulder stretch – with right elbow pointed to the ceiling, touch upper back with right hand and grab rt elbow with left hand – pull
    g. With left elbow pointed to the ceiling, touch upper back with left hand and grab elbow with right hand – pull
    h. (longer than 10 seconds) Hanging arm circles – bend at waist, keep back straight, let one arm hang freely. Rotate that one arm 10 X clockwise and 10 X counterclockwise gradually increasing the radius of each circle. Repeat with other arm. Brace with unused arm during stretch if necessary.

i. Standing trunk twist – grab elbow from side and pull. Rotate trunk in same direction. Repeat on opposite side. Hold each for 5 seconds.

j. Wall push offs – touch the wall with the tip of your shoe. Measure 2 shoe lengths back (2 “ft”) from the wall. Stabilize ft at this mark and perform 5 push offs while touching your forehead or top of head (avoiding O_2 mask hits) to the wall with each repetition.

k. Wall calf stretch – touch the wall again with one shoe and touch the knee of that leg to the wall, leave the other shoe 2 ft away from the wall. Without lifting the heel of either shoe, lean against wall to stretch calf muscle. Hold for 10 seconds. Repeat with the other foot.

l. Stand around until the 63 (and subsequently 73, 83, and 93) minute mark is reached. Mount the Echo Bike.

m. Place your shoes on the foot pegs, perform push pull in very minimal fashion for one minute (i.e. 10 Watts on the display).

n. Place shoes on foot pedals. Continue minimal movement of pedals.

o. Repeat sequence, start over with sitting on the floor and reaching to the ceiling OR if at the 95-minute mark, return to your seat.

p. 55 minutes of rest now occur in the seated position with minimal movement.

10) At timepoint 150 minutes, pressure-altitude flight profile begins!

Summary of timepoints:

T = 0 minutes; Pre-breathe 100% oxygen on pilot mask begins

T = 5 minutes; Approximation of time to mount Echo Bike and begin 85% HRmax exercise

T = 20 minutes; Approximation of 10 minutes total at target HR

T = 25 minutes; Dismount bike, drink water, towel off if necessary, take a seat

T = 55 minutes; Minimal exercise portion, begin by sitting on floor and reaching for the ceiling

T = 95 minutes; Return to seat, Principal Investigator may inspect instrumentation

T = 145 minutes; Chamber resealed

T = 150 minutes; Pressure-altitude flight to 30K’, pilot mask removed and PAX mask applied

T = 154 minutes; Continue ascent to 45K’ for data collection

Watts	kcal·hr^{-1}	mL O_2·kg^{-1}·min^{-1}	L·min^{-1}	% $\dot{V}_{O_2,peak}$
0.00	91.6	4.4	0.305	9.7
6.46	113.8	4.8[1]	0.379	12.0
8.81	121.8	5.8[2]	0.406	12.9
14.90	142.8	6.8[3]	0.476	15.1
20.59	162.5	7.7	0.542	17.2[4]
21.59	166.0[5]	7.9	0.553	17.6
25.00	177.9	8.5	0.593	18.8
28.17	189.0	9.0	0.630	20.0
50.00	266.3	12.7	0.888 (0.9)	28.2
100.00	449.1	21.4	1.497 (1.5)	47.5
139.66	600.0	28.6	2.000	63.5
150.00	640.2	30.5	2.134 (2.1)	67.7
155.45	661.5	31.5	2.205	70.0
167.44	708.8	33.8	2.363	75.0
200.00	839.5	40.0	2.798 (2.8)	88.8
225.68	945.0	45.0	3.150	100.0
250.00	1047.0	49.9	3.490 (3.5)	110.8

Table 8: Metabolic rates during exercise as reported.(Gerth, 2018) Yellow highlighted data from Table 9.5 in Astrand, et al.(Astrand P.O. Rodahl, 2003) Green highlighted data indicates metabolic rate specified and experimentally found (average) regarding light and heavy exercise within CEVIS studies

Appendix A6. POST-flight Subject Assessment and Release Instructions

Completed morning of Subject experimentation after informed consent

Subject ID #: _____ Age (18 to 50): _____

1. Return to ground level and continue to breathe through PAX mask until indicated by IO or Principal Investigator. For the first 30 minutes at 10-minute intervals, Subjects will be monitored by IOs for signs/symptoms of DCS. Subjects will also be constantly aware of any pain, niggles, anomalies and will inform IOs of any abnormal personal assessments.
2. Follow IO instructions – expectedly PAX mask will be removed at timepoint 15 minutes elapsed at ground level at which time water can be ingested.
3. Between 15 and 30 minutes, a blood draw and weighing will likely occur.
4. 30 minutes after arrival at ground level, Subjects and/or IOs may shower using room temperature water. Hot showers are contra-indicated as risk of DCS increases. Alternatively, Subjects may relocate outside of the chamber yet remain under observation.
5. Between 30- and 60-minutes following return to ground level – Chamber is completely de-crewed and prepared for next flight.
6. One last DCS assessment is performed by IOs.
7. 60 minutes after return to ground level, Subject release from CAMI with instructions:
    a. Refrain from strenuous activity for 12 hours
    b. Avoid alcohol consumption for 12 hours
    c. Valsalva frequently throughout the night (clear ears and flex torso as if defecating) – Draegar ear is not expected but be aware of inner ear pressure and equilibrate often
    d. Be aware of potential signs/symptoms as listed in Appendix A7, review with IOs last thing before departure
        i. Report to your employer any signs/symptoms in order that Baptist Integris may be informed to therefore communicate and activate the appropriate response according to the expert medical opinion provided.

Appendix A7. Analysis and Calculations Description Continued

SpO_2 data

Curve “C” is affiliated with the coding of performance classification that was presented on page 8, *Passenger Oxygen Mask* section. It is simply a graphical representation of minimal oxygen delivery values in liters per minute under normal temperature pressure dry conditions (NTPD; 20 degrees Celsius, sea level pressure of 1 atmosphere [760 mmHg], and very minimal to no moisture). Minimal oxygen flow was defined in this study as maintaining an SpO_2 of 80.75% as determined experimentally as a 14,000’ base line equivalent for each Subject.

Breathing volume data (i.e., respiration rate and minute volume)

Every 1500 rows within the generated Excel spreadsheet represented one minute’s time. As no post-experiment analysis tools were available for expansion strap analysis, the following Excel equations were generated to describe breathing functions at the conclusion of every altitude/oxygen flow scenario. Row 316798 data is used in this example. AG$550000 and AQ$550000 number values are critical for placement beyond the last row of data.

- AG column recorded scaled combined expansion strap volumes (mL)
- Peaks and valleys were established in column AR with:
  - =IF(AND(AG316798>AG316796:AG316797:AG316794:AG316795:AG316792:AG316793:AG316790:AG316791:AG316788:AG316789, AG316798>AG316799:AG316800:AG316801:AG316802:AG316803:AG316804:AG316805:AG316806:AG316807:AG316808), "Peak", IF(AND(AG316798<AG316796:AG316797:AG316794:AG316795:AG316792:AG316793:AG316790:AG316791:AG316788:AG316789, AG316798<AG316799:AG316800:AG316801:AG316802:AG316803:AG316804:AG316805:AG316806:AG316807:AG316808), "Valley", ""))
- If an event peak or valley occurred, it was recorded as an event in column AQ
  - =IF(AR316798="peak", 1, IF(AR316798="valley", 2, ""))
- Events were observed in column AP to then generate “exhale low volumes”
  - =IF(AQ316798=1, INDEX(AG316798:AG$550000, MATCH(2, AQ316798:AQ$550000, 0)), "")
- “Total one breath (mL)” was then calculated in column AO
  - =IF(AQ316798=1, AG316798 - AP316798, "")
- As breaths are unlikely to occur as whole events on the minute scale, partial breaths were accounted for using these next equations for “blanks near anchor value to 1st value” and “blanks far 1500 rows up” respectively column AJ and AK
  - =IF(AV316798=1, ROW() - LOOKUP(2, 1/(INDIRECT("Ao1:Ao" & ROW()-1)<>""), ROW(INDIRECT("Ao1:Ao" & ROW()-1))), "")

        - =IF(AV316798=1, COUNTBLANK(OFFSET(AO316798, -MIN(ROW()-1,1499), 0, MATCH(1, INDEX((AO316798: INDEX(AO:AO,ROW()-MIN(ROW()-1,1499))<>"")*1, 0), 0)-1)), "")
    - An uncorrected volume of breaths were then calculated that occurred within the minute prior to concluding the experimental scenario in column AL
        - =IF(AV316798=1, SUM(FILTER(AO316798:INDEX(AO:AO,ROW()-MIN(ROW()-1,1499)), (AO316798:INDEX(AO:AO,ROW()-MIN(ROW()-1,1499))<>""))), "")
    - This finding was then corrected using the extra cells (partial breaths) and additionally corrected for the pneumotach/expansion strap ratio that was calculated using PFT data and located in AS440 in this example
        - =(AL316798/(1500-AK316798-AJ316798)*1500)/AS440
    - Breaths per minute were calculated
        - =COUNTIF(AQ315298:AQ316798,1)-1
    - These calculations would only activate when notes were taken and marked in LabVIEW that then populated specific scenario descriptions in column AW with a “1” being a marker placed in column AV

Heart Rate -- descriptive statistics only (i.e., means, standard deviations, etc.)

Average and standard deviation were calculated via MS Excel in similar fashion to breathing calculations. At the conclusion of each experimental scenario a note was dropped via LabVIEW describing said scenario in column AW and a “1” was marked in column AV.

- 1500 rows (1 minute) average heart rate per alt/o2 bpm equation
    - =IF(AV316798=1, AVERAGE(FILTER(AH316798:INDEX(AH:AH,ROW()-MIN(ROW()-1,1499)), (AH316798:INDEX(AH:AH,ROW()-MIN(ROW()-1,1499))<>""))), "")
- Associated standard deviation
    - =IF(AV316798=1, STDEV.S(FILTER(AH316798:INDEX(AH:AH,ROW()-MIN(ROW()-1,1499)), (AH316798:INDEX(AH:AH,ROW()-MIN(ROW()-1,1499))<>""))), "")

Appendix B. Informed Consent to Participate in Research Study

Appendix B. Title: Optimized Flow Oxygen Systems (OFOS) – Passengers

Statement of Research

It is a basic ethical principle that an individual who voluntarily participates in a research study must give his or her informed consent prior to such participation. This consent must be based on the understanding of the purpose and risks of the research. This informed consent document provides important information for understanding the purpose and risks of this research study. Research projects include only participants who voluntarily choose to participate. Please take your time to make your decision. If at any time you have questions, please ask the principal investigators or a member of their research staff.

Invitation to Participate in Research Study

Dr. James Campbell, Dr. Susan Jay and researchers at the FAA's Civil Aerospace Medical Institute (CAMI), invite you to participate in a research study regarding adequate passenger oxygen supplementation at various altitudes. This study is funded by the U.S. Government.

Key Information

- Your participation in this study is voluntary. Refusal to participate is well within your rights and will involve no penalty or loss of benefits to which you are otherwise entitled.
- You must read the information that follows and ask questions about anything that you do not understand before deciding whether to participate. Drs. Campbell and Jay must also consider INCLUSION and EXCLUSION CRITERIA, listed in detail in this form, to fully assess your status before allowing enrollment in this study.

Purpose of the research
– This FAA study seeks to provide data that will allow modification to oxygen systems design rules and regulations. Provided data are expected to reveal performance-based, physiological metrics of blood oxygen saturation (SpO_2) levels that show equivalence or superiority to current guidance. The two main goals specified on p.10 of the protocol both support the overall objective of establishing a human-performance based quantitative indicator of adequate supplemental oxygen supply at altitude.

Expected duration of the prospective subject's participation
– You will participate in one chamber flight that is expected to last 8.5 hours or less.

Procedures to be followed in the research
– Physiological data acquisition sensors will be placed at several different sites: 1) an elastic band around your chest for heart rate measurement, 2) near infrared sensors (NIRS) on a finger, forehead, wrist, and additional location, 3) tubing lines from your passenger (PAX) mask to measure partial pressure of gases in real time, and 4) expansion bands will be placed on the lower chest and abdomen for breathing rate and volume estimation (list of sensors not exclusive). A simulated 45,000 ft altitude flight will occur for which a hypobaric

(low-pressure) chamber will be utilized. Subsequent 5,000 ft descent increments will be studied. Supplemental oxygen will be provided.

The reasonably foreseeable risks or discomforts to the prospective subject
– with chamber exposure of significant low pressure and duration comes minimal but possible risk of decompression illness (similar in fashion to SCUBA diving), yet this protocol includes recompression treatment as procedural regardless of any signs/symptoms of decompression illness.

– you will be airlocked into a hypobaric chamber that has about as much internal space as a school bus. Much like a school bus, one must wait for the bus to stop and safety arrangements to be made before disembarking. If you are agoraphobic or claustrophobic, this is not a protocol in which you should participate.

– discomfort may come in the way of: extended time of mask wearing, work of breathing, remaining seated for hours, exercise on an unfamiliar piece of equipment, pressure changes may trigger pain in sinuses, gastrointestinal tract or dental areas, dehydration, less than opulent restroom facilities, and instrumentation with resulting restricted movement.

The benefits to the prospective subject or to others that may reasonably be expected from the research
– Subjects, that will all be 3rd class medical certificate holders or higher, will be trained in an environment for which they may find themselves during future emergency operations for which these Subjects will gain a personal perspective of oxygen supply challenge at high altitude.

- This translates into a better prepared and trained pilot/crew/air traffic controllers for a safer National Air Space.
- This translates into a greater knowledge and experience that can then be shared with other professionals in the aviation field that improves safety in the National Air Space.

– aid in justification of regulatory guidance modifications that can be incorporated into aircraft oxygen systems design (expected to allow manufacturer's design liberty and testing simplification/focus to improve hypoxia protection for all passengers [safety])

– promote more efficient air travel [higher altitudes, less oxygen reagent = less weight, less air traffic congestion, less fuel burned]

– benefits of exercise are readily accepted in the scientific and medical fields.

– measures will be available on the very slight chance that decompression illness signs/symptoms (the bends as it is called in SCUBA diving) occur and do not resolve.

– Subjects will be monetarily compensated.

– Subjects will be maintained in a hyperoxic state for which thousands of cancer and wound patients find accelerated recovery.

Description of participant involvement

If you agree to participate in this study, your involvement will last approximately 8.5 hours. Performance of this protocol will occur at the Civil Aerospace Medical Institute (CAMI), building 13 atrium located at 6500 South MacArthur Oklahoma City, Oklahoma.

In the first 30 minutes, you will be provided with a brief by the principal investigator followed by Subject screening to assure compliance with necessary research criteria (INCLUSION, EXCLUSION, and pre-flight preparation), will give a blood sample (approximately $1/20^{th}$ or less of the volume of a normal donation) and, if blood hematocrit and hemoglobin qualify, then you will transition to the CAMI Research Hypobaric Chamber (Blue). The research team will be available to respond to questions or concerns about the research study and to ensure safety of all involved.

The altitude chamber simulates the effects of high altitude on the human body by lowering pressure in controlled and calculated fashion. There you will be given guidance from a qualified instructor about the altitude chamber and the sequence of events that will take place. Flight depressurization testing (ear check) and SpO_2 baselining at 10,000 ft and 14,000 ft pressure-altitude will follow.

A risk-minimizing pre-flight exercise protocol will be performed immediately following #2. Pure oxygen will be breathed via a demand-type mask. Clinical stress-test level exercise will be performed on a Rogue Fitness Echo Bike for approximately 15 minutes that will be followed by rest and additional very light movement for 40 minutes. Total pre-breathe protocol time will be 2.5 hours.

You will participate in one pressure-altitude simulated flight in an enclosed and sealed hypobaric chamber at approximately 74 °F. For this study, maximum chamber pressure-altitude is 45,000’; 0.143 atmospheres pressure for a maximum of 10 minutes. Subsequent lower pressure-altitudes will follow for maximum times of 15 or 20 minutes each. Simulated altitude will not exceed 45,500’, total “flight” time will be approximately 3 hours, and total chamber time will be approximately 7 hours. In every tested scenario, supplemental oxygen will be provided yet may be temporarily decreased or removed (after maximum pressure-altitude has been reached to make certain no additional nitrogen loading occurs/DCS risk remains minimal). The system of oxygen supply will be swapped between on-demand vs. PAX mask phase-dilution as designed upon ascent or if necessary during flight to maintain adequate SpO_2 of 60% or above.

Subjects will return to approximately ground level pressure-altitude for observation/questioning/additional blood draw.

One may not want to participate due to the difficulty that will be experienced at the highest altitude where oxygen will be lesser available than at lower altitudes. The sensation will not be similar to holding one’s breath, in fact respiratory drive may fluctuate from fast to slow breathing depending upon the accelerated off-gassing of carbon dioxide at altitude. Alternatively, one may want to participate for the same reason, to feel the effects of hypoxia and gain greater knowledge of that human state.

One may not want to participate due to the significant pressure drop that will be experienced. Those that have digestive issues, aggressive gas production, gastroesophageal reflux disease

and the like will find acting as a Subject for this research to be unpleasant. A list of suggestions and EXCLUSION CRITERIA can be found within the protocol.

Audio/Video/Picture capture are not required for data collection for this project. Documentation is extremely beneficial for presentation and record-keeping descriptors to then allow for research reproduction as is critical to the scientific method. Concurrence for such record keeping would be appreciated.

Time requirements summary:

Screening (approx. 30 minutes) - For screening purposes, you will be asked to complete a medical history form. A brief physical screening will be conducted the morning of the chamber flight to ascertain that basic INCLUSION CRITERIA are truly met.

Subject depressurization testing (approx. 30 minutes) - After you are approved for chamber flight participation, you will transition to the hypobaric chamber for flight to 10,000 and 14,000 ft pressure-altitude and then return to ground level. This excursion is expected to take less than 30 minutes.

Pre-breathe with exercise (approx. 150 minutes) - This portion of flight preparation involves continuous breathing of oxygen and two bouts of exercise: one vigorous exertion for about 15 minutes (10 minutes in a heart rate zone of near 85% max) and one very light exertion for 40 minutes.

Chamber flight (approx. 180 minutes) – Figure 2 in the research protocol illustrates the flight profile. This phase begins with ascent to 30,000 ft pressure-altitude at which point the on-demand oxygen mask is swapped for a passenger (PAX) mask. Ascent then continues to 45,000 ft for which SpO_2 data are collected. Subsequent changes in pressure-altitude will follow as a series of descents to 40,000, 35,000, 30,000, 25,000, 20,000, 18,500, 15,000, and 12,000 ft. Each altitude will last no longer than 20 minutes. Time at 45,000 ft will not exceed 10 minutes.

Ground level dwell (up to 120 minutes but no less than 60 minutes) – Subject observation/questioning will follow chamber flight to assure no signs of decompression illness are present.

Potential Benefits

Direct benefits to you as a subject in this research may be gained as an increase in knowledge and understanding of oxygen supply challenges at high altitude. The information gained from this study will enable a better understanding of passenger oxygen need during an emergency decompression event and will aid the development of regulatory guidance that can be incorporated into aircraft oxygen systems design and manufacture to improve hypoxia protection and promote more efficient air travel (higher altitudes = less air traffic congestion and less fuel burn in turbine engines for covering equivalent distances). Additional benefits are summarized in bullet point format in the key information section above.

Risks and discomforts

As with most research protocols, this protocol involves risks that you should carefully consider before agreeing to participate.

Hypobaric exposure

- Trapped gas within the human body may expand causing discomfort or pain: Subjects are strongly advised to adhere to a diet that minimizes digestive tract gas formation as doing so will minimize this risk of trapped gas expansion. The CIA prescribed diet for U2 pilots which can be almost completely absorbed from the gastrointestinal tract (minimize poop creation) includes: coffee, rice, eggs, meat, cottage cheese, noodles, sweets, and soups. General advice is to avoid beans, lentils, cabbage, broccoli, cauliflower, bok choy, brussel sprouts, bran, dairy, sorbital, soda, beer, carbonated beverages, fruits and vegetables. However, know thyself is better guidance as digestive disorders are the main cause of gas formation, unique to each individual. Boyle's Law allows us to calculate the expansion of gas for any given pressure change. As occupants of the chamber will transition from 1 atmosphere of pressure to 0.143 atm, a trapped gas of 1 liter would become 7 liters at altitude. Guidance to avoid sodas and gas-producing food prior to hypobaric experimentation cannot be overemphasized.
- Decompression sickness/illness: an aggressive pre-breathe procedure (exercise + pure oxygen) has been adopted for this protocol in which risk of DCS is being minimized.
    - On the very slight chance that decompression illness occurs, an automatic repressurization treatment plan is in place to counter further development of signs/symptoms and poor clinical outcomes.

A full description of risks, discomforts, and protocol interventions to minimize risks may be found in Appendix A3A, A3B, A3C, A4, and A5. A summary of the science underlying the risk can be focused down upon two major players: oxygen and nitrogen.

- The oxygen component risk comes from the lack of overall ambient pressure that exists at altitude that is simulated with a hypobaric (low-pressure) chamber. Dalton's Law of Partial Pressures helps us understand that the sub-component gasses of air remain in the same ratios at lower pressures, yet these components still are additive to the total pressure. Much fewer molecules of oxygen are therefore available in the same volume of air at altitude and therefore hypoxia is a veritable risk. This OFOS protocol mitigates this risk by supplying more than adequate oxygen at every altitude to be able for the human to perform "regular" operations and function. However, at altitudes above 41,500 ft, 100% oxygen delivery does not meet metabolic need. At this altitude, Subjects should expect to become hypoxic, SpO_2 values as indicated on the finger (as you may have seen in a hospital) and on the head (for this study) will drop. The highest altitude studied therefore necessitated additional mitigation for which the chamber altitude will decrease (pressure will be increased in the control room) and pressurized oxygen will be delivered if/when an SpO_2 of 60% is reached. This is expected to occur in all Subjects within 60 seconds and recovery measures are automatically prescribed.

- The nitrogen component risk also comes from lack of pressure, yet as nitrogen is an inert gas. It is therefore not consumed by the body, as is oxygen, and acts in similar fashion to carbon dioxide in soda when exposed to lesser pressure (opening of a soda can). Henry's

Law specifies the amount of gas dissolved in a liquid is proportional to its partial pressure above the liquid. Nitrogen bubbles form in everyone who transitions from a high pressure to a lower pressure. The size and number of bubbles that form are mathematically related to the pressure differential experienced and the time frame in which the total pressure change occurs. Mitigation for SCUBA divers occurs with decompression stops. This OFOS study performs a 100% oxygen pre-breathe that "washes out" nitrogen from its respective compartments (tissue, organs, blood) down its concentration gradient. This OFOS study uses exercise to minimize nucleation sites at which nitrogen bubbles may form. NASA uses this combination prescription to allow extravehicular activity (spacewalks, spacesuit operations) for which NASA has extensively studied the components, metabolic load, and time of effort thoroughly to the point of optimal avoidance of decompression sickness for space missions. OFOS uses the NASA prescribed pre-breathe with exercise to avoid the nitrogen bubble component risk and uses equivalency for time at altitude exposure to determine acceptable limits that are equally acceptable by NASA and the US Navy (less than 2% risk of DCS Type I and less than 0.1% risk of DCS Type II).

If a participant experiences significant physiological distress (needle stick, mask discomfort, lack of intestinal fortitude, etc.), testing will be stopped, and the participant will be removed from the hypobaric chamber. Inside Observers will be in the chamber to monitor and evaluate the participant, and any necessary assistance will be provided.

There is always a risk of loss of confidentiality associated with participating in a research study. All records containing personal identifiable information are kept in locked cabinets and password-protected computers in secure locations. The risk of loss of confidentiality is minimal. Nonetheless, the researchers involved in this study will take every precaution necessary to ensure your privacy is protected.

Alternative Procedures or courses of treatment

You may choose not to participate at all. Refusal to participate or to continue to participate will not harm or influence your class issued of your FAA first-class medical certificate.

Compensation

- The government shall have no obligation to pay you or your employer for the time or travel fees for prospective subjects that present with falsely credited INCLUSION CRITERIA, i.e.) non-possession of a 3rd class medical, BMI above 40, a smoker, not between the ages of 18 and 50, and/or anemic.
- The government expects two (2) hours' equivalent pay to be allocated by your employer for each acceptable subject according to INCLUSION CRITERIA (hematocrit and hemoglobin values not included) delivered to MMAC who participates in an experimental testing session.
- The government expects a minimum of three (3) hours' equivalent pay to be allocated by your employer for Subjects that pass all INCLUSION CRITERIA and EXCLUSION CRITERIA that apply to the point of ear pressure check.

- The government expects your employer will provide a minimum of four (4) hours' equivalent pay for Subjects that achieve the 45,000-foot mark (thereby indicating that Subject was able to successfully complete the 15-minute exercise portion of EXCLUSION CRITERIA).
- The government expects your employer will provide eight (8) hours' equivalent pay for Subjects that are able to achieve a full successful flight (thereby indicating that Subject was able to successfully complete all of EXCLUSION CRITERIA including not being opposed to giving the final blood sample or sitting for the necessary duration of the post-flight observation period to collect "all physiological data and any medical records generated during any procedures associated with the full experimental testing session").

Participant's Rights

The FAA's Civil Aerospace Medical Institute (CAMI) Institutional Review Board, which is responsible for the ethical conduct of human subjects research performed by FAA researchers, has reviewed this research study and found it to be acceptable, according to applicable state and federal regulations designed to protect the rights and welfare of research participants.

Cost to Participant

You will be responsible for the cost of your transportation to and from the research study, as well as any other expenses incurred (e.g., lodging, meals, etc.).

If you experience significant physiological distress, testing will be stopped and (you) the participant will be removed from the hypobaric chamber. Medical personnel will be onsite to monitor and evaluate you. In the unlikely event, basic first aid and/or advanced cardiac life support (ACLS) will be provided. As each Subject is not an independent contractor but rather an employee, transportation to a recompression hyperbaric facility and treatment will be provided in the unlikely event of decompression illness signs/symptoms by your employer.

During or after this research, medical treatment will be provided to you by your employer if you require such treatment as a result of participation in the study, as soon as such need is recognized. Except for medical treatment, no special compensation is available for injuries you might incur during participation in this research. If at any time you believe that participating in this research has injured you and appropriate care or redress has not been provided, you may discuss possible remedies with your employer.

Confidentiality

The data and information that you provide during the course of this research are confidential. No personally identifiable information, data, or statements will be disclosed in any report, briefing, presentation or discussion of the research **unless such information is required to be disclosed under the Freedom of Information Act (FOIA),** ***5 U.S.C. § 552***, **or otherwise required to be disclosed by law**. ***Information, data, or statements subject to FOIA may be protected from release if it falls within one of the nine FOIA exemptions. Such exemptions include the protection of personally identifiable information (PII) under exemption b(6) when such information would constitute a clearly unwarranted invasion of personal privacy of the individuals involved. However, de-identified information data, or statements***

may still be disclosed under FOIA. The de-identified data may also be made available to other researchers for research-related purposes only.

- All records associated with your participation in the study will be subject to the usual confidentiality standards applicable to medical records (e.g., such as records maintained by physicians, hospitals, etc.), and in the event of any publication resulting from the research no personal, identifiable information will be disclosed. Therefore, your research data will NOT be linked to your FAA medical records data. The researchers code your data with an identification number for statistical analyses. All records containing personal identifiable information will be kept in locked cabinets and/or password-protected computers in secure locations.
- Over the course of experimentation and at conclusion, research studies occasionally are evaluated by Institutional Review Boards (IRB) and other oversight agencies (i.e., Department of the Navy Human Research Protection Program, Food and Drug Administration, Office for Human Research Protections) to determine that the study was conducted properly. If such an evaluation is requested for this study, information about subjects will remain confidential to the greatest extent possible.
- We can assure you that your name will not be linked to any information collected in the study. However, the fact that you are participating in this study will or may become known to people that you personally inform.
- Your privacy will be protected to every possible extent, but CAMI personnel will come in contact with you as a Subject in accordance with their official duties. This information will not be shared outside of the CAMI facility.
- De-identified information from this study may be shared with other government/military research entities or universities as part of the data analysis process and is required to be posted to a public information repository. Your identity will not be linked to any of the information.
- Specimens for hematocrit/hemoglobin parameters will be discarded after use.
- Study information that could identify Subjects will be maintained according to law.
- Paperwork will be minimal. Any paperwork that exists will be digitized and original documents will be shredded by a secure commercial shredding company 5 years after completion of the study.
- Photo/Video data collected during research has the potential for use in presentations and will be held ad infinitum. No photos/videos will be taken of a given Subject without consent.

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that certain people or groups may inspect and copy records pertaining to this study. Examples of other people or groups are the Federal Aviation Administration's Office of Aerospace Medicine Institutional Review Board. This is a committee that reviews and approves research studies for the protection of Human Subjects. Some of these records for review could contain personal information that identifies you. Reasonable efforts will be made to

keep your personal information contained in the research record private and confidential. However, absolute confidentiality cannot be guaranteed.

Injury

Every effort to prevent injury as a result of your participation will be taken. It is possible, however, that you could develop complications or injuries as a result of participating in this research study. In order to cover the risk of injury, your employer shall provide insurance coverage sufficient to cover medical expenses related to treatment of injuries sustained by Subjects during their participation in this project.

Voluntary nature of the study

Significant new findings related to your personal health discovered during the course of this research which may or may not relate to your willingness to continue participation may be provided to you by a CAMI physician. You may voluntarily terminate or withdraw from any research described in the Protocol without penalty or loss. If you decide to withdraw from this research, you will notify your employer that will then notify the Principal Investigator at (405) 954-5517 to ensure an orderly and safe termination process.

a) Testing (chamber flight) will be terminated for the day if any test participant (Subject or Inside Observer) cannot complete the pre-breathe protocol as designed.
b) Testing will be terminated (during flight) if any test participant (Subject or IO) exhibits signs/symptoms of mild to moderate DCS. Treatment IS return to ground level – 100% oxygen will be provided via an aviator's mask at this time as well as has been AF procedure despite a NASA report stating that it has little effect.
c) Testing will be terminated (during flight) if any test participant (Subject or IO) exhibits signs/symptoms of severe DCS (that will be treated with return to ground level – 100% oxygen will be provided via an aviator's mask at this time with additional immediate start of transfer for Hyperbaric Chamber treatment likely at Baptist Integris Hospital: *phone #405-949-3320, address 3300 NW Expressway OKC 73112.*
d) Testing will be terminated if the Subject reports feeling unwell or has an unexplained loss of consciousness (LOC). An immediate emergency descent profile will be performed as soon as AAM-400 personnel can prepare, and it is safe to proceed. Any such afflicted individual will be placed on 100% oxygen (if not already breathing 100% oxygen) and the medical monitor notified.
e) A standard descent profile (5000 ft/minute) will be performed for any participant who states that they no longer want to continue with the chamber flight.

Any test participant who reports or shows visible signs of DCS or aborts voluntarily from a chamber flight will be unenrolled from the study and their data removed from subsequent hypothesis-driven statistical analysis. Data may still be used in deidentified descriptive analysis. Any Subjects that report feeling unwell or lose consciousness on two separate days will be unenrolled from the study and data gained may be used for descriptive analysis but not hypothesis-testing statistical analysis. Any Subjects that request removal from the study for any or no reason will be handled according to arrangements specified in the recruitment literature.

Participation and Withdrawal

Your participation in this study is completely voluntary and it is your choice whether to participate or not. You may decline or withdraw participation from the study at any time. The

choice to decline or withdraw from the study will not cause any penalty or loss of any benefit to which you are entitled and will not jeopardize your access to care, treatment and health services. If you decide to stop participating, please speak with Dr. James Campbell and/or Dr. Susan Jay, Principal Investigators, who will tell you how to stop safely and who will discuss with you the follow-up care which could be most helpful for you.

Dr. James Campbell or Dr. Susan Jay may decide to stop or withdraw you from the study under certain circumstances without your permission. Some possible reasons that you may be removed from the study include risk or harm to your medical or psychological interest; not following the study instructions, or administrative reasons. In the event that your participation in the study ends early, you may request or you may be requested to speak to the principal investigator.

At any time during this research study, the principal investigator or research team may share any new information that may affect your health or well-being. Your continued participation in the study may be impacted and may therefore require further discussion.

With the expectation that you agree to the multitude of information above, the following are necessary characteristics and data points that potential participants must meet to subsequently be allowed to enroll as a Human Research Subject for the Low/ Optimized Flow Oxygen Systems study.

Subjects must fall within the following INCLUSION CRITERIA parameters:

- Possess and present a current FAA 3rd class medical certificate or higher (non-expired on day of experiment)
- Be between the ages of 18 and 50 years on the day of enrollment
- Be a non-smoker, non-vaper
- have a BMI < 40 according to initial weight and height
- Must have hemoglobin (Hb) and hematocrit (HCT) values of $\geq$ 12.0 g/dL and $\geq$ 37% respectively on day of altitude chamber flight as determined by pre-flight CAMI blood draw (INCLUSION CRITERIA here will be that the Subject has no known anemia, is currently not menstruating, and has not given blood/plasma/platelets in the last 30 days). Of course, for a Subject to continue into the research chamber, the Hb and HCT value limits must be met or exceeded.

Contractor-supplied Subjects must not fall within the following EXCLUSION CRITERIA parameters:

- Any medical/clinical respiratory condition (e.g., asthma, chronic obstructive pulmonary disease [COPD], etc.)
- Any cold, acute upper respiratory infection (URI), or respiratory issue within two (2) weeks prior to study participation
- Any neuromuscular disease, neuropathy, peripheral vascular disease, hypertension, or Raynaud’s Phenomenon/Syndrome

- Have medical conditions or physical limitations that would preclude them from a 15-minute bout of vigorous exercise or to experience an altitude decompressive/recompressive event.

  *** Disqualifying medical/physical conditions to include: respiratory ailments such as asthma or emphysema; pregnancy; hypo/hypertension; diagnosed heart problems; chest pains, difficulty breathing; serious bodily disability, deformity, or dismemberment; spells of severe dizziness; diabetes requiring medication; claustrophobia; recent surgery; or any other chronic disease.

- Men or women that are sensitive to other's touch or uncomfortable in enclosed environments must not volunteer to be subjects for this study.
- Anyone that brings headgear/earbuds, cell phones, rings or bracelets to the CAMI laboratory check-in as these items are included/discussed in the "no personal items" clause in the contract. Simply refrain from bringing unnecessary personal belongings to CAMI.
- Taking any medication or drug which may impair physical or cognitive activity, or which precludes the operation of heavy machinery/driving.
- Actively under the influence of recreational drugs or intoxicated due to alcohol consumption.
- Afraid of needles or be opposed to giving blood. Subjects should attend with the full intention of supplying data described in the Optimized Flow Oxygen Systems human subject research protocol including blood samples.
- History of corrective eye surgery or detached retina.
- Unable to understand, be illiterate in, or unable to follow directions presented in written and spoken English language.
- Unwilling to provide accurate personal information such as age, education level, previous flying experience, etc., to be used for research purposes.
- Unwilling to have anthropomorphic measurements recorded, such as height, weight, girth, etc. for research purposes.
- Does not arrive or takes objection to wearing "tennis shoes/sneakers" with comfortable non-restrictive exercise-friendly clothing that allows for instrumentation access, (e.g., red-dot stickers for electrocardiograph [EKG] signal acquisition, watch placement on wrist, finger probe access, etc. A sports bra for all female Subjects is highly encouraged, not only to allow for athletic movement, but also for bare skin access that is necessary for research sensor placement while preserving modesty. Several chest/abdominal straps will be placed around the torso and will remain in place for the duration of the experimental session.
- Subjects uncomfortable with the fact that there are no female Inside Observers/chamber personnel. Inside Observers are medical/health science professionals that may need to

place and/or re-adjust red dot sensors or chest/abdominal straps attached directly to the skin. Some of these sensors/instrumentation devices will be placed in the chest area.

- Unwilling to complete a health history questionnaire. The Principal Investigator must review the form for scientific criteria and, if necessary, consult with a medical expert regarding Subject safety before clearing a volunteer Subject for participation.
- Unwilling to allow the FAA access to all physiological data and any medical records generated during any procedures associated with the full experimental testing session as well as access to any medical records post-testing session on the very slight chance that medical treatment is required due to study participation. By human subject protections rules, Institutional Review Boards must be informed of UPIRTSOs (Unanticipated Problems Involving Risk to Subject or Others). Appropriate description of (if) and extent of (quantitation) any unanticipated event should be reportable with accurate data.
- Physically unable to participate in a simulated altitude decompression event while remaining calm and under self-control without endangering themselves or others.
- Unenergetic and does not possess the stamina to wear oxygen masks that may promote a level of discomfort when worn for several hours.
- Subjects must not report with:
    - Painted fingernails (including clear coat)
    - Any coloration on fingers (magic marker or pen ink/tattoos)
    - Any facial hair including beards or mustaches
    - Body odor or smelly clothes/shoes
    - Intestinal gas (pay attention to your diet several days in advance

*** For Subjects that have been allowed to participate in the OFOS study, discovery of disqualifying changes to INCLUSION CRITERIA status after achievement of Subject status will be considered EXCLUSION CRITERIA rather than protocol deviations: med. certs may expire, hematocrit may not be of sufficient value, Subject may take up unfortunate habits (smoking), etc.

Contact Information

If you have any scientific or ethical questions about the research, you may contact:

Dr. James Campbell

6500 South MacArthur Blvd, AAM-631, Bldg. 13, Room 155B, OKC, OK 73169-6918

or Dr. Susan Jay

6500 South MacArthur Blvd, AAM-631, Bldg. 13, Room 155C, OKC, OK 73169-6918

Email: 9-amc-physiology@faa.gov

If you have any questions/concerns as a subject in a research study, about research itself, and/or rights and use of identifiable information, you can speak to the study team, Chair or any

member of the Institutional Review Board (IRB). In the event of a research-related injury, contact your employer.

Medical Monitor will be contracted.

Subjects may contact the PI (scientific/ethical questions) or the Contract company/your employer (work related questions) at any time.

If you have questions about the study, please ask before signing this form. However, you can ask any questions that you have about this study at any time.

Signature and Consent to be in the OFOS research study

I have been informed about the purpose, procedures, possible benefits and risks of this research study. I have read (or someone has read to me) this form, and I have received a copy of it. I have had the opportunity to ask questions and to discuss the study with an investigator. My questions have been answered to my satisfaction. I have been told that I can ask other questions any time. I voluntarily agree to participate in this study. I am free to withdraw from this study at any time without the need to justify my decision. The withdrawal will not in any way affect my future treatment or medical management and I will not lose any benefits to which I am otherwise entitled. I agree to cooperate with the principal investigator and the research staff and to inform them immediately if I experience any unexpected or unusual symptoms.

____ I understand the risks and benefits of this research and agree to participate.

Below, I have indicated my decision about being re-contacted for related studies in the future by placing an “X” next to my choice:

___ Yes, please contact me about related studies

___ No, please do NOT contact me about related studies

Participant: By signing this consent form, you indicate that you are voluntarily choosing to take part in this research.

_____

Printed Name of Participant

_____

Name of Legal Representative (if applicable)

_____ _____

Signature of Participant or Legal Representative Date